# EMERGENCIES IN THE COVID ERA

# The consequences of the Covid-19 pandemic on elective surgery for colon cancer



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# The consequences of the Covid-19 pandemic on elective surgery for colon cancer

AIM OF THE STUDY: This study presents the impact of the Covid-19 pandemic on elective surgical treatment of patients diagnosed with colon cancer, in a University Clinic of Surgery.

MATERIAL AND METHODS: The data from patients who underwent an elective surgery procedure for colon cancer during the pandemic period (26.02.2020-01.10.2021) was analyzed. This period was compared with the same interval for the years 2016-2017 and 2018-2019.

RESULTS: There was a significant decrease in the number of patients that underwent an elective surgery for colon cancer during the pandemic. The Covid-19 generated pandemic has influenced the number of days from diagnosis to treatment, preoperative and postoperative hospitalization. There was an increase in the number of patients with severe symptoms, with complete or incomplete ileus. The number of lymphatic nodes harvested increased during the last period of study, being correlated with the advanced cancer stage.

CONCLUSIONS: The Covid-19 pandemic had an influence on the management of the patients with colon cancer undergoing an elective surgery procedure. Firstly, their number decreased compared to the other periods, and they presented more severe symptoms. The duration of the surgical act was extended, but the postoperative stay was shortened.

KEY WORDS: Colon cancer, Covid-19 Pandemic, Duration of surgery, Elective surgery

# Introduction

Colon cancer represents the third most common form of cancer in male patients and the second most common in female patients. This pathology is responsible for 10% of all types of tumoral malignancies worldwide. Approximately 600,000 deaths occur annually worldwide due to this pathology, placing colon cancer in the fourth

place of cancer mortality <sup>1,2</sup>. At the level of the European Union, the 5-year survival rate varies from 28.5% to 57% in men and from 30.9% to 60% in women <sup>3</sup>. The risk of developing colon cancer is linked with two broad categories of factors: behavioral factors and genetic factors. An increase in the incidence of this pathology has been observed in the countries where the adoption of the "Western" lifestyle was more obvious <sup>4</sup>. In these countries, the rates of obesity, alcohol consumption, red meat consumption, smoking, sedentary lifestyle, have risen significantly, contributing to the development of colon cancer.

The treatment and management of all cancers was massively influenced by the appearance of the SARS CoV-2 virus in Wuhan, China, which spread all over the world, with the first case confirmed in Romania on

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February 26, 2020. The World Health Organization has declared the disease a global pandemic, making it a public health emergency. This pandemic has produced major changes in the lifestyle of the population around the world as well as in the management of their other diseases. People were restricted from leaving their houses, even physician and hospital visits were reduced, and patients were guided by the authorities to request medical help only in case of severe symptoms, as most of the hospitals' efforts were focused on treating patients with Covid-19.

# Aim of the study

Our study intends to analyze the influence of the Covid-19 pandemic on the elective surgical treatment of the patients diagnosed with colon cancer, comparing the pandemic period (26.02.2020-01.10.2021) with the same time intervals of 2016-2017 and 2018-2019.

## Materials and Methods

The study included patients diagnosed with colon cancer, diagnosed by colonoscopy and biopsy on outpatient basis, who underwent a surgical procedure in the First Surgery Clinic of the Pius Brinzeu Clinical Emergency County Hospital in Timisoara (one of the three surgery clinics of a large, regional hospital).

The study has included patients admitted between February 26, 2020, and October 1, 2021, and the corresponding time intervals from 2016-207 and 2018-2019, respectively. Several inclusion and exclusion criteria were applied. The inclusion criteria were the following: patients undergoing elective surgery for the treatment of colon cancer, with the diagnosis of colon cancer previously established by colonoscopy and biopsy, the location of the tumor varying from cecum to the level of the rectosigmoid junction. For the last period, during the Covid-19 pandemic, we have used additional inclusion criteria: lack of any symptoms suggesting Covid-19 infection in the last seven days, and a negative SARS-CoV-2 PCR test upon hospital admission. The exclusion criteria were: patients undergoing emergency surgery due to colon cancer, lack of diagnosis made by colonoscopy and outpatient biopsy, or location of the tumor at another level than the previously mentioned. The additional exclusion criteria applied to the period 2020-2021 were: the presence of any symptom characteristic for Covid-19 infection in the last seven days (as the patients underwent a proper epidemiological triage at hospital admission), or a positive PCR test performed on the day of admission.

The data collection was performed after obtaining the agreement from the Ethics Commission of the Hospital. The following parameters were recorded: the patient's

date of birth, gender, place of origin (urban or rural), the hospital admission date, the number of hospitalization days, the number of days from diagnosis to surgery, the number of days from hospitalization to surgery, the duration of surgery, the duration of postoperative hospital stay, the presence of mild symptoms (such as bloody stool, melena, increasing frequency of defecation) or severe cancer symptoms (such as abdominal pain, emesis, reduced flatulence and hemorrhage of the lower digestive tract). The associated pathologies of the patients were also considered, together with the Charlson Index. The location of the tumor was classified, as tumors located in the cecum, ascending colon, liver angle were defined as tumors belonging to the right colon, while those located in the splenic angle, descending colon, sigmoid colon, and the rectosigmoid junction were defined as tumors belonging to the left colon; transverse colon tumors were considered separately, and recurrence status was also recorded.

The types of surgical interventions were divided into right colectomies, left colectomies, transverse segmental resections, and other colectomies. Regarding these interventions, the technique applied to perform the anastomosis was analyzed, considering if it was performed manually using thread sutures, or it was made mechanically with the stapler, as well as if the intervention needed a protective stoma. The surgery type was classified as radical or palliative and the presence of postoperative complications was also analyzed.

Other studied parameters included the presence/absence of complete/incomplete ileus, whether the tumor had invaded adjacent organs, and the patient's need to be monitored in intensive care. The values of the Carcinoembryonic Antigen (CEA) were analyzed as well. From a pathological point of view, the histological type of the tumor, the degree of invasion (T), the number of dissected nodes and the number of nodes with metastases (N), the presence or absence of metastases (M), the presence of lympho-vascular invasion and the cancer stage were considered. Status during hospital discharge (healed, improved, stationary, aggravated, deceased) was also one recorded.

# STATISTICAL ANALYSIS.

The IBM SPSS Statistics for Windows program was used to analyze all the collected data. Determination of mean, standard deviation and median was used for continuous variables that had a normal distribution, these variables being analyzed using independent sample tests. Regarding the variables that did not have a normal distribution, they were analyzed using medians and percentiles. When it came to analyzing the categorical variables that have been presented as cases and percentages, the Chi-square tests were used, with a p<0.05 indicating a statistically significant difference in the study.

#### Results

During the studied time period, 147 patients underwent elective colon cancer surgery. Over the three periods of time (between 2016 and 2021), this represents 3% of all patients that underwent elective surgery in our Surgery Department. The demographical results are presented in (Table I).

The patients were aged between 37 and 87 years, the average age being 65.75 years, the standard deviation 9.98 years, and the median 66 years.

During the Covid-19 pandemic, 29 interventions were performed, representing 19.72% of the total number of cases, compared to 68 (46.25%) in 2018-2019 and 50 (34.01%) in 2016-2017. The variations of the tumor

TABLE I - Demographical aspects

	N	(%)
Gender	Male Female	78 (53%) 69 (47%%)
Environment	Urban Rural	104 (70.74%) 43 (29.25%)

locations as well as the type of surgery to which the patient was subjected during the three periods are presented in (Table II).

An essential parameter of the study was the duration of surgery over the three periods - its variation is presented in (Table III).

The curative intent of the surgery was analyzed: in 2016-2017, 41 patients (82%) benefited from a curative treatment and nine patients (18%) underwent palliative surgery. In the period 2018-2019, 57 patients (83.82%) received curative treatment and 11 patients (16.17%) benefited from a palliative treatment. During the pandemic, 28 patients (96.55%) received curative treatment and just one patient (3.44%) underwent palliative surgery.

During the period 2016-2017 there were five patients (10%) with recurrent tumor, in the period 2018-2019 there were 11 patients with recurrent tumor (16.17%), and during the pandemic there were two patients (6.89%) with recurrent tumor.

The different types of anastomosis and the postoperative complications are presented in Table IV.

The protective stoma in 2016-2017 was performed in five cases (10%), in 2018-2019 in six cases (8.82%), and during the pandemic in four cases (13.8%).

Table II - Variations of tumor location and surgery type over the three periods

		2016-2017	2018-2019	2020-2021
Tumor location	Right colon (%)	18 (36%)	18 (26.47%)	9 (31.03%)
	Left colon	27 (54%)	40 (58.82%)	18 (62%)
	Transverse colon	5 (10%)	10 (14,7%)	2 (6.89%)
Intervention type	Right colectomy	18 (36%)	18 (26.47%	9 (31.03%)
,,	Left colectomy	19 (38%)	40 (58.82%)	18 (62%)
	Segmental resection of transvers colon	5 (10%)	6 (8.82%)	2 (6,89%)
	Other colectomies	8 (16%)	4 (5.88%)	0

TABLE III - Duration of surgery

	169	2016-2017	2018-2019	2020-2021
Surgery duration (minutes)	Average (minmax)	165.38(60-330)	193.44(90-390)	230.21(90-420)
	Standard Deviation	59.56	68.16	82.39
	Median	155.5	180	225

After Chi square test: p<0.001 between all 3 periods compared; p<0.001 for 2018-2019 compared to 2020-2021

TABLE IV - Anastomosis techniques and complications

		2016-2017	2018-2019	2020-2021
Anastomosis technique	Manual with threads	34 (68%)	48 (70.58%)	12 (41.73%)
	Mechanic with stapler	11 (22%)	14 (20.58%)	13 (44,82%)
Postoperative complications	Total	5 (10%)	13 (19.11%)	2 (6.89%)
	Intestinal fistula	2 (4%)	4 (5.88%)	1 (3.44%)

After Chi square test: p=0.03 between all 3 periods compared; p=0.025 for 2018-2019 compared to 2020-2021

Table V - Type of symptomatology

		2016-2017	2018-2019	2020-2021
Symptomatology	Mild	45 (90%)	49 (72.05%)	18 (62.06%)
	Severe	5 (10%%)	19 (27.94%)	11 (37.93%)

After Chi square test: p=0.02 between all 3 compared periods

TABLE VI - TNM staging and cancer stages

		2016-2017	2018-2019	2020-2021
TNM	$T_1$	-	4 (5.88%)	
	$T_2^{'}$	5 (10%)	5 (7.35%)	4 (13.79%)
	$T_3^2$	30 (60%	37 (54.41%)	16 (55.17%)
	$egin{array}{c} T_3 \ T_{4a} \end{array}$	12 (24%)	14 (20.5%)	7 (24.13%)
	$T_{4b}^{\tau_a}$	3 (6%)	8 (11.76%)	2 (6.89%)
	$N_0$	28 (58%)	34 (50%%)	17 (58.62%)
	$N_1^{\circ}$	14 (28%)	14 (20.58%)	7 (24.12%)
	$N_2^{'}$	8 (16%)	20 (29.41%)	5 (17.24%)
	$M_0$	40 (80%)	60 (88.23%)	29 (100%)
	$M_1^{\circ}$	10 (20%)	8 (11.76%)	0
After Chi square: p= 0.016 for 2016-20 Number of harvested lymph nodes	Average (min-max)	20.5 (4-34)	18.61 (2-57)	20.21 (5-45)
7 1	Median	25.5	15	17.5
	SD	7.73	12.64	9.96
Lymph nodes with metastasis	Average (min-max)	1.73 (0-11)	2.86 (0-17)	2.54 (0-13)
	Median	0	0	0
	SD	3.16	4.5	3.75
	At least one with metastasis	36%	42.64%	44.80%
Lymphovascular invasion	Yes	23 (46%)	26 (38.23%)	15 (51.72%)
, 1	No	27 (54%)	42 (61.76%)	14 (48.27%)
Cancer Stage	I	10 (20%)	8 (11.76%)	4 (13.79%
	II	20 (40%)	21 (30.8%)	11 (37.93%)
	III	12 (24%)	28 (41.17%)	14 (48.28%)
	IV	8 (16%)	11 (16.17%)	0
After Chi square test: p= 0.047 between .	2016-2017 and 2020-2021			

TABLE VII - Evaluation of different hospitalization durations

		2016-2017	2018-2019	2020-2021
Days from diagnosis to surgery	Average (minmax)	15.58 (1-62)	27.36 (1-183)	25.35 (2-120)
	SD	14.68	25.13	30.17
	Median	12	20	13
Days from hospital admission to surgery	Average (min-max)	4.38 (1-10)	3.82 (1-9)	4.29 (2-9)
	SD	2.26	1.92	2.03
	Median	4	3	4
PostoperativeDays	Average (min-max)	12 (5-35)	14.58 (4-99)	11.17 (3-33)
	SD	5.27	14.4	6.66
	Median	10	10	9
Total days of hospitalization	Average (min-max)	16.21 (9-39)	18.18 (9-102)	14.33 (4-35)
	SD	6.11	14.33	6.94

Intensive care during hospitalization was also taken into account: in 2016-2017, no patient required postoperative monitoring in the intensive care unit, in 2018-2019 in three patients (4.41%) there was a need for postoperative hospitalization in the intensive care unit, while in 2020-2021 four patients (13.79%) were admitted in intensive care. The severity of patients' symptomatology (mild or severe) is presented in (Table V).

The presence of ileus was considered: in 2016-2017 only three patients (6%) presented with subocclusive syndrome, during 2018-2019, there were seven patients (10.29%) with subocclusive syndrome, while during the pandemic there were three patients (10.34%) with subocclusive syndrome, and four patients with occlusive syndrome (13.79%).

After analyzing the proportions of the presence of sub-occlusive syndrome or occlusion, the Chi square test was applied, resulting in a p=0.049 between 2016-2017 and 2020-2021, and in a p=0.025 between 2018-2019 and 2020-2021.

Patients' co-morbidities were analyzed using the Charlson Index. The average value of the Index in the period 2016-2017 was 4.02 (min. 2 - max. 8), with a standard deviation (SD) of 1.87 and a median value of 3. In the period 2018-2019 the index had an average value of 3.51 (min. 2 - max. 9), with a SD of 1.9 and a median of 3. During the pandemic, the Charlson Index had an average of 3.21 (min. 2 - max. 6), a SD of 1.02 and a median of 3.

From a pathological point of view, in all the three periods,  $G_2$  differentiated moderate adenocarcinoma was predominant, in the period 2016-2017 being present in 74% of cases, in the period 2018-2019 in 61.76% of cases and in the period 2020-2021 in 79.31% of cases. Data on the TNM staging and cancer stage over the three periods presented in (Table VI).

The presence of tumor infiltration of adjacent organs was considered: in the period 2016-2017, in eight cases (16%) there were one or more adjacent organs infiltrated; in the period 2018-2019, 17 patients (25%) had tumor infiltration in other organs, while during the pandemic, there were six patients (20.68%) with tumor infiltration

The average value of the CEA tumor marker was 25.7 ng/mL in the period 2016-2017, 15.66 ng/mL in the period 2018-2019, and 27.33 ng/mL during the pandemic

In order to establish the influence of the pandemic on the elective treatment of colon cancer, parameters such as the duration from diagnosis to surgery, duration of preoperative hospital stay, duration of postoperative hospital stay, and total duration of hospitalization were analyzed and presented in (Table VII).

Discharge status during the three periods was finally investigated: in the period 2016-2017, all 50 patients (100%) were declared cured; in the period 2018-2019, 59 patients (86.76%) were declared cured at discharge,

six patients (8.82%) were declared improved and three patients (3.68%) have died. During the pandemic, 27 patients (93.1%) were declared cured, and two patients (6.9%) have died.

#### Discussion

The pandemic has generated a series of extraordinary measures for the health system to deal with the cases of infection. Health systems around the world have focused on the treatment of the patients infected with SARS-CoV-2, while the rest of the pathologies were neglected at least in the first phases of the pandemic.

In the period 2020-2021, only 29 patients (19.72%) underwent elective surgery for colon cancer, representing a 42% reduction in the number of cases operated during 2016-2017, and a 57.3% reduction compared with 2018-2019.

This was mainly due to the initial advice of the authorities to go to the hospital only in case of severe symptoms or surgical emergencies, the intensive care units being directed to the treatment of patients with Covid-19 infection, as on March 16, 2020, a "state of emergency" was introduced in Romania.

Also, the fear of patients to contact the virus in the hospital environment, was another factor worth considering. As for the future, the number of colon cancers patients is expected to increase, as they were not diagnosed during the pandemic.

The severity of the pathology is higher, due to the postponement of the screening as well as the postponement of the surgery. In Italy, the number of patients diagnosed with cancer in secondary care units was 39% lower in 2020 than in 2018 and 2019 <sup>5</sup>.

The duration of the surgical intervention has increased during the 3 periods, and this can be observed by its average value, varying from 165.38 minutes in 2016-2017 to 230.21 minutes during the pandemic.

Following the statistical analysis of this parameter between the periods 2016-2017 and 2020-2021, it has resulted a p <0.001, which means there is a very significant difference between the two periods. Comparing the period 2018-2019 with 2020-2021, a p<0.001 was obtained again, showing very significant differences between the two periods. This longer time of surgery is explained by the patient's preparation in the operating room, which is prolonged due to increased safety measures against infection with the SARS-CoV-2 virus, more careful isolation of the operating field, and equipping staff with additional protective equipment. Other similar studies have shown statistically significant differences between the pandemic period and the years before, with a p=0.002 <sup>6-8</sup>.

surgical therapy with curative intent was mainly indicated to the patients in the study thus, in the first two periods, 82% and 83.82%, respectively, benefited from

curative treatment while during the pandemic, 96.55% of the patients benefited from curative treatment it should be noted that during the pandemic, all stage iv patients were redirected to the oncology department during the three studied periods, recurrent cases increased from 10% to 16.17% in the first two periods, and decreased by more than half to 6.89% during the pandemic.

The analysis of the type of intestinal anastomosis has shown some interesting differences: in the first 2 periods, the mechanical anastomosis using a stapler was used in 22% and respectively 20.58% of cases, while during the pandemic, it was used in 44.82% of cases (p = 0.03). This increase was due both to the evolution of the surgical technique and to the surgeons decision to avoid postoperative complications, trying to shorten the hospital stay during the pandemic. however, current international studies show that the mechanical anastomosis is used in at least 77% of the cases, a figure which is higher than the one presented in this study  $^9$ . Nonetheless, we can witness an obvious increase in the adoption of this method, as presented above.

By analyzing the proportions of patients admitted in the intensive care unit with the chi square test, a p=0.045 was obtained, resulting in statistically significant differences: in the period 2016-2017, no patient was admitted in the intensive care clinic, but the percentage increased to 4.41% in the period 2018-2019 and to 13.79% in the period 2020-2021. This increase was mainly due a precaution of the attending physicians, which preferred that the patient is better monitored during the initial postoperative stay, in order to reduce the complications rates.

The proportion of patients with more severe symptoms at hospital admission was higher during the pandemic (37.93% vs. 10% and 27.94%, respectively; p=0.02), and higher than the one previously reported in the literature (over 20%), due to the restrictions imposed by the authorities, as well as to the accentuation of the fear for SARS-CoV-2 infection in the hospital, which convinced the patients to postpone their visits to the doctors <sup>6</sup>. Patients' comorbidities were assessed using the Charlson Comorbidity Index. Its average value ranged from 4.02 in the first period to 3.51 in the second and to 3.21 in the pandemic.

The presence of the lowest rate of complications during the pandemic may be due to the fear of patients with comorbidities to visit hospitals. In order to be operated, they had to perform outpatient investigations, which involved additional visits to health facilities and therefore a prolonged virus exposure risk.

Thus, those with multiple comorbidities decided to protect themselves, preferring to postpone all these procedures for a while.

There was an increase in the average number of dissected lymph nodes, which may be due to the improvement of the surgeons' technique, and also a higher percentage of stage  $N_1$  and  $N_2$  patients during the pandemic, which implies a wider excision of the lymph nodes, due to the complexity of the case. The increase of the number of harvested lymph nodes was observed also in other studies  $^5$ . It should be noted that the average of metastatic lymph nodes increased in parallel with the average of resected lymph nodes, and with the degree of lymph node invasion.

During the pandemic period, patients with stage IV were mainly redirected to the Oncology Departments. In this period there was no patient admitted with metastases, while in 2016-2017, 20% of cases had metastases, and implicitly Stage IV. Following the statistical analysis, performed on the first period (2016-2017) and on the pandemic period to highlight the proportions of patients with metastases obtained, a p = 0.016 has shown that there are significant differences between proportions. This is similar to other studies, which also show significant differences <sup>10,11,12</sup>. During 2016-2017, the patients presented in 40% cases with cancer stages II and III, 38.23% during 2018-2019, and 48.28% during the pandemic (p=0.047).

The mean value of the CEA tumor marker varied from 25.7 ng/mL to 15.66 ng/mL to 27.33 ng/mL over the three periods. This variation can be justified by differences in the screening process: in the first period colonoscopy and biopsy were procedures that were less used, due to the small number of locally available devices - they were used in cases with more severe symptoms, which often involved a more advanced stage of cancer. With the increase in the number of colonoscopies and biopsies and the quality of screening, tumors were detected earlier, and these procedures were performed on patients with milder symptoms, due to easier access to investigations between 2018 and 2019. During the pandifficulty of performing outpatient the colonoscopy with biopsy, due to the limiting of the movement of patients away from home, and to the fear of contact with the new coronavirus, led to predominantly higher stage presentations, with a higher CEA value. The literature also confirms an increase of the CEA values 6.

The time from diagnosis to treatment was also influenced by the Covid-19 pandemic.

Although the number of cases has, the number of days required from diagnosis to treatment remained was 25.35; other studies also showed longer durations between diagnosis and treatment during the Covid-19 pandemic <sup>13</sup>. Moreover, this increased duration correlated negatively with the duration from hospital admission to surgery (p=0.047), and with the number of lymph nodes subjected to pathological examination: as the delay in treatment increases, the patient's situation worsens, requiring a shorter preoperative hospitalization period, and increasing the number of lymph nodes suspected of invasion.

The duration from hospital admission to surgery has

increased during the pandemic to 4.29 days, compared to 3.82 days in 2018-2019. This increase was due to precautionary measures taken by health institutions to limit infection with Sars CoV-2 virus.

The duration of the postoperative stay decreased from 14.58 days during 2018-2019 to 11.17 days during the pandemic. This shortening was explained by the measures implemented to reduce the risk of SARS-CoV-2 infection, so when patients were hemodynamically stable, had intestinal movements, and with no fever, they were discharged.

The postoperative complications were reduced from 19.11% in 2018-2019 to 6.89% during the pandemic, a decrease of more than two and a half times. Also, the stay in the postoperative intensive care unit was shortened, which led to a decrease of postoperative hospital stay. International studies show a decrease of postoperative hospitalization from an average of 12.1 days in 2018 to 9.6 days during the pandemic, confirming our results <sup>14</sup>.

Death toll rose from 3.68% before the pandemic to 6.9% during the pandemic. This increase was due to the presentation of patients with more advanced symptoms, and a more advanced stage of cancer.

#### **Conclusions**

During the pandemic, the number of patients who underwent elective surgery for colon cancer has decreased significantly. There were also significant differences regarding the duration of the surgical intervention, as the pandemic period was associated with the longer durations. There were more patients with severe symptoms presenting during the pandemic period, while the duration from diagnosis to the moment of the surgical intervention was increased. The duration of hospital stay was significantly reduced, in order to minimize the risk of the patients to being infected with the SARS-CoV-2 virus in the hospital.

As for the future, the number of colon cancers patients is expected to increase, as they were not diagnosed during the pandemic because of the restrictions imposed by authorities and because of the fear of the patients to visit the medical institutions.

## Riassunto

La pandemia Covid-19 ha influenzato la gestione e il trattamento in chirurgia elettiva dei pazienti con cancro al colon. Questo periodo ha generato un decremento del numero dei pazienti sottoposti a trattamento chirurgico e, al tempo stesso, un incremento degli stessi con sintomatologia più severa. Anche la durata stessa dell'atto chirurgico ha sofferto, il numero di giorni dalla diagnosi al trattamento, dal ricovero all'operazione, la degenza

postoperatoria ne hanno risentito. Il cancro al terzo stadio è stato il più comune durante la pandemia e si è assistiti ad un importante incremento dell'uso delle anastomosi meccaniche.

Ci si aspetta, in futuro, che il numero dei pazienti con cancro al colon aumenterà, per il semplice fatto che essi non sono stati diagnosticati durante la pandemia a causa delle restrizioni imposte dalle autorità e della loro paura e riluttanza a venire in contatto con presidi ospedalieri per evitare il contagio con il virus SARS-CoV-2.

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