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Impact of the COVID-19 Pandemic on Colorectal Cancer Care in the Netherlands: A Population-based Study

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Abstract

The COVID-19 pandemic disrupted health care services worldwide. This study aimed to investigate the impact of the pandemic on colorectal cancer care in the Netherlands. In total, 1,653 colorectal cancer patients diagnosed in 25 hospitals in weeks 2 to 26 of 2020 were selected from the Netherlands Cancer Registry. The impact on colorectal cancer care in the Netherlands was limited.

Introduction: The COVID-19 pandemic disrupted health care services worldwide. In the Netherlands, the first confirmed COVID-19 infection was on February 27, 2020. We aimed to investigate the impact of the pandemic on colorectal cancer care in the Netherlands. Methods: Colorectal cancer patients who were diagnosed in 25 hospitals in weeks 2 to 26 of the year 2020 were selected from the Netherlands Cancer Registry (NCR) and divided in 4 periods. The average number of patients treated per type of initial treatment was analyzed by the Mantel-Haenszel test adjusted for age. Median time between diagnosis and treatment and between (neo)adjuvant therapy and surgery were analyzed by the Mann Whitney test. Percentages of (acute) resection, stoma and (neo)adjuvant therapy were compared using the Chi-squared test. Results: In total, 1,653 patients were included. The patient population changed during the COVID-19 pandemic regarding higher stage and more clinical presentation with ileus at time of diagnosis. Slight changes were found regarding type of initial treatment. Median time between diagnosis and treatment decreased on average by 4.5 days during the pandemic. The proportion of colon cancer patients receiving a stoma significantly increased with 6.5% during the pandemic. No differences were found in resection rate and treatment with (neo)adjuvant therapy. Conclusion: Despite the disruptive impact of the COVID-19 pandemic on global health care, the impact on colorectal cancer care in the Netherlands was limited.

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Keywords: Colon, Rectal, Treatment, (neo)adjuvant therapy, Resection, Stoma

Introduction

The coronavirus disease 2019 (COVID-19) was first diagnosed in Wuhan, China, and is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In the Netherlands, the first confirmed COVID-19 infection was on February 27, 2020. After this, the coronavirus spread fast through the whole country. To prevent COVID-19 from spreading any further, the Dutch government has taken various societal measures such as social distancing, closing stores and schools, and urging people to only leave their homes when necessary.

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The COVID-19 pandemic also had a major impact on the health care services worldwide. Patients who were infected with the coronavirus were prioritized within the health care services. Furthermore, the Dutch official authorities suggested to only visit the general practitioner (GP) with serious complaints. This led to a situation in which patients were less likely to go to the GP with complaints, leading to a lower number of patients being diagnosed with cancer during the COVID-19 pandemic. Moreover, national screening programs were halted due to the COVID-19 pandemic, including the screening program for colorectal cancer in the Netherlands from mid-March 2020 to mid-May 2020. Studies showed that the number of colorectal cancer diagnoses dropped mainly in the age group eligible for screening, 55 to 75 years, during the COVID-19 pandemic.

In the beginning of March 2020, the Foundation of Oncological Cooperation (SONCOS) and the Dutch Association for Medical Oncology (NVMO) published the first recommended measures on how to deal with the COVID-19 pandemic within health care services in the Netherlands. Examples of the recommended measures for colorectal cancer care were postponing surgery after neoadjuvant therapy and adjuvant therapy after surgery, to adjust the planned elective care during the COVID-19 pandemic.

The aim of this study was to investigate the impact of the COVID-19 pandemic on colorectal cancer care in the Netherlands in 2020 and whether patients received treatment according to the recommended measures published for colorectal cancer care during the COVID-19 pandemic.

Methods

Patients

Patients ≥18 years diagnosed with colorectal cancer during weeks 2 to 26 of 2020 were included in this study. Data were selected from the Netherlands Cancer Registry (NCR) and derived from 25 of the 70 hospitals in the Netherlands, consisting of 10 general hospitals, 11 large teaching hospitals and 4 academic hospitals spread throughout the Netherlands. For patients included in this study, the following data were gathered: patient characteristics (eg, age at diagnosis, gender, performance status, and comorbidity), tumor characteristics (eg, clinical stage, pathological stage, and ileus), type of treatments (eg, systemic therapy, radiotherapy, and resection), interval between different events (eg, number of days between diagnosis and initial treatment), as well as the hospital where the patient’s received treatment.

Definitions

For all patients, age at diagnosis was grouped into ages <55, 55 to 75 and ≥75 years.

The selected period was divided in 4 periods based on national data requested from the nationwide network and registry of histopathology in the Netherlands (PALGA): period A, weeks 2 to 8 (ie, before the COVID-19 pandemic); period B, weeks 9 to 11 (ie, COVID-19 pandemic before screening program was halted); period C, weeks 12 to 17 (ie, COVID-19 pandemic with more than 25% of the expected amount of screening colonoscopies); and period D, weeks 18 to 26 (ie, COVID-19 pandemic with less than 25% of the expected amount of screening colonoscopies). To analyze treatment with adjuvant therapy and time between surgery and start of adjuvant therapy, patients were divided in these 4 periods based on date of surgery. For all other analyses, patients were divided in these 4 periods based on date of diagnosis.

The Eastern Cooperative Oncology Group (ECOG) Scale of Performance Status (PS) was used for performance status.

TNM classification (7th edition) was used for staging the tumors. For colon cancer, the pathological stage was used if available and otherwise clinical stage, while for rectal cancer, clinical stage was always used.

Hospitals where patients received their treatment for colorectal cancer were categorized into different regions in the Netherlands: North/East, South and West. The regions were defined to investigate whether there were regional disparities regarding the impact of the COVID-19 pandemic.

Statistical Analysis

The baseline characteristics of included patients were tested by Chi-squared tests to determine significant differences between patients diagnosed in period B, C, and D of the year 2020 separately compared to period A of 2020.

To analyze type of initial treatment, the average weekly incidence of patients per type of initial treatment was calculated by type of cancer, tumor stage and period. The average weekly incidence in period B, C, and D was separately compared with the average weekly incidence in period A using the Mantel-Haenszel test adjusted for age.

The median time between diagnosis and initial treatment was calculated by type of cancer, region, and period. The median time between neoadjuvant therapy and surgery was calculated for patients with clinical stage II or III rectal cancer by type of neoadjuvant therapy and period. The median time between surgery and adjuvant therapy was calculated for patients with stage III colon cancer by period. All median times of period B, C, and D were separately compared with period A using the Mann Whitney test.

Proportions of patients who underwent a resection and received a stoma were calculated by type of cancer, tumor stage and period. Also, the proportion of patients treated with neoadjuvant therapy was calculated for patients with stage II or III rectal cancer by type of neoadjuvant therapy and period. For patients with stage III colon cancer, the proportion of patients treated with adjuvant therapy was calculated by period. Here, all proportions of period B, C, and D separately as well as combined were compared with period A using the Chi-squared test.

Stata version 16.1 software was used to analyze all data and for all tests performed, and a 2-sided P-value of <.05 was considered statistically significant.

Results

Research population

In total, 1,653 patients were included, with a total number of 410, 161, 231, and 385 colon cancer patients in period A to D, respectively. Corresponding numbers of rectal cancer patients among the 4 periods were 174, 68, 84, and 140, respectively. The baseline characteristics are presented in Table 1a (colon cancer) and Table 1b (rectal cancer).
The proportion of colon and rectal cancer patients aged 55 to 75 years was lower in period D ($P < .01$) compared to period A. The proportions of patients diagnosed with colon cancer stage I or II were lower in period C ($P = .04$), and D ($P < .01$) compared to period A. Furthermore, the proportion of colon cancer patients presenting with ileus was higher in period C and D than in period A, 13.9% and 14.3% versus 8.0% respectively. Finally, the proportion of rectal cancer patients with a good performance status was significantly lower in period D compared to period A, 37.1% versus 51.1% respectively.

### Type of Initial Treatment

Differences between type of initial treatment among the different periods are summarized in Figure 1A (and Supplementary Table A.1) for colon cancer patients and in Figure 1B (and Supplementary Table A.2) for rectal cancer patients.

A significant increase in the weekly average number of resections per week was observed in patients aged >75 years with colon cancer stage I, aged <55 years with colon cancer stage III, aged >75 years with colon cancer stage III, and all ages with colon cancer stage IV. By contrast, the weekly average number of resections significantly decreased in patients aged 55 to 75 years and diagnosed with colon cancer stage III. For all ages and colon cancer stage II, the weekly average number of patients who underwent resection with construction of a stoma on the same day significantly increased. Finally, a significant increase of the average number of local excisions was observed in clinical stage I rectal cancer patients >75 years of age. In rectal cancer patients diagnosed with clinical stage II, III, or IV, no significant differences in type of initial treatment were found between the different periods.

### Time Between Diagnosis and Initial Treatment

In colon cancer patients, the median time between diagnosis and initial treatment was significantly shorter in period C and D compared to period A; 14 days and 20 days versus 23 days, respectively (Supplementary Figure A). Regarding regional disparities, the median time until initial treatment was significantly shorter in periods B, C, and D compared to period A for the region North/East (Supplementary Figure A) and was significantly shorter in period C.
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Table 1B: Characteristics of Patients Diagnosed With Rectal Cancer in Periods A, B, C, and D of 2020.

| Patients | Period A N (%) | Period B N (%) | P-value | Period C N (%) | P-value | Period D N (%) | P-value |
|----------|----------------|----------------|---------|----------------|---------|----------------|---------|
| Age (years) |                |                |         |                |         |                |         |
| <55      | 29 (16.7)      | 11 (16.2)      | .46     | 8 (9.5)        | .27     | 23 (16.4)      | <.01    |
| 55-75    | 102 (58.6)     | 45 (66.2)      |         | 51 (60.7)      |         | 60 (42.9)      |         |
| >75      | 43 (24.7)      | 12 (17.6)      |         | 25 (29.8)      |         | 57 (40.7)      |         |
| Gender   |                |                |         |                |         |                |         |
| Men      | 121 (69.5)     | 44 (64.7)      | .47     | 52 (61.9)      | .22     | 72 (51.4)      | <.01    |
| Woman    | 53 (30.5)      | 24 (35.3)      |         | 32 (38.1)      |         | 68 (48.6)      |         |
| ECOG PS  |                |                |         |                |         |                |         |
| 0        | 89 (51.1)      | 35 (51.5)      | .66     | 38 (45.2)      | .49     | 52 (37.1)      | .03     |
| 1        | 28 (16.1)      | 12 (17.6)      |         | 15 (17.9)      |         | 37 (26.4)      |         |
| 2-4      | 13 (7.5)       | 7 (10.3)       |         | 3 (3.6)        |         | 11 (7.9)       |         |
| Unknown  | 44 (25.3)      | 13 (19.1)      |         | 28 (33.3)      |         | 40 (28.6)      |         |
| Comorbidity |            |                |         |                |         |                |         |
| No       | 74 (42.5)      | 29 (42.6)      | .92     | 39 (46.4)      | .88     | 54 (38.6)      | .60     |
| One      | 51 (29.3)      | 19 (27.9)      |         | 23 (27.4)      |         | 39 (27.9)      |         |
| Two      | 19 (10.9)      | 6 (8.8)        |         | 9 (10.7)       |         | 20 (14.3)      |         |
| Unknown  | 30 (17.2)      | 14 (20.6)      |         | 13 (15.5)      |         | 27 (19.3)      |         |
| Clinical stage |       |                |         |                |         |                |         |
| Stage I  | 52 (29.9)      | 26 (38.2)      | .53     | 23 (27.4)      | .35     | 32 (22.9)      | .54     |
| Stage II | 37 (21.3)      | 9 (13.2)       |         | 10 (11.9)      |         | 26 (18.6)      |         |
| Stage III| 52 (29.9)      | 18 (26.5)      |         | 31 (36.9)      |         | 50 (35.7)      |         |
| Stage IV | 27 (15.5)      | 12 (17.6)      |         | 17 (20.2)      |         | 26 (18.6)      |         |
| Stage X  | 6 (3.4)        | 3 (4.4)        |         | 3 (3.6)        |         | 6 (4.3)        |         |
| Ileus    |                |                |         |                |         |                |         |
| No       | 137 (78.7)     | 51 (75.0)      | .74     | 64 (76.2)      | .94     | 93 (66.4)      | .90     |
| Yes      | 4 (2.3)        | 2 (2.9)        |         | 2 (2.4)        |         | 3 (2.1)        |         |
| Unknown  | 33 (19.0)      | 15 (22.1)      |         | 18 (21.4)      |         | 44 (31.5)      |         |
| Region   |                |                |         |                |         |                |         |
| North/East |       |                |         |                |         |                |         |
| South    | 80 (46.0)      | 29 (42.6)      | .77     | 42 (50.0)      | .14     | 63 (45.0)      | .72     |
| West     | 53 (30.5)      | 20 (29.4)      |         | 31 (36.9)      |         | 48 (34.3)      |         |

Period A, week 2 to 8; Period B, week 9 to 11; Period C, week 12 to 17; Period D, week 18 to 26; ECOG, Eastern Cooperative Oncology Group; PS, Performance Status. The P-value was calculated excluding missing values, using the Chi-squared test to compare patients diagnosed in period B, C or D of 2020 with patients diagnosed in period A of 2020.

Compared to period A for the region South and West (Supplementary Figure A).

In rectal cancer patients, the median time between diagnosis and initial treatment was significantly shorter in period C compared to period A; 23 days versus 30 days, respectively (Supplementary Figure B). No significant differences were found for the region North/East (Supplementary Figure B). However, the median time was significantly shorter in period B for the region South (Supplementary Figure B) and in period C for the region West (Supplementary Figure B) compared to period A.

Time Between (Neo)adjuvant Therapy and Surgery

No significant differences were found among the different periods regarding the median time between neoadjuvant chemoradiotherapy and surgery (Supplementary Figure C), the median time between neoadjuvant radiotherapy and surgery (Supplementary Figure C), and the median time between surgery and adjuvant therapy (Supplementary Figure D).

Treatment

The proportions of patients treated with (acute) resection, stoma, and (neo)adjuvant therapy are shown in Table 2a (colon cancer) and Table 2b (rectal cancer).

A significantly higher proportion of colon cancer patients underwent an acute resection in period C (8.4% and 8.4%), period D (9.6% and 5.5%), as well as combined periods B to D (7.7% and 6.2%) if compared to period A (5.3% and 2.6%).

In the combined periods B to D, 18.7% of colon cancer patients received a stoma versus 12.2% in period A. If analyzing period C and D separately, a significant higher proportion of stoma construction of 19.5% and 18.7% respectively, was found if compared to 12.2% stomas in period A.

Analyzing the use of neoadjuvant therapy (radiotherapy and/or chemoradiation) and the administration of adjuvant therapy did not reveal any significant differences for the different periods.

Discussion

This population-based study investigated the impact of the COVID-19 pandemic on colorectal cancer care in the Nether-
lands. Despite the disruptive impact of the COVID-19 pandemic on global health care, the impact on colorectal cancer care in the Netherlands was found to be limited. However, only slight changes were shown.

First of all, the patient population changed during the COVID-19 pandemic. Our results show that in period C and D, colon cancer patients more often presented with ileus or underwent an acute resection. This might be a reflection from the national recommendation to visit the GP only with serious complaints.4,6 Another possible explanation is the temporary halt of the colorectal cancer screening program4,5. Indeed, less tumors were diagnosed in the population eligible for screening during the COVID-19 pandemic,6 resulting in a relative overrepresentation of symptomatic cancers.

Due to the COVID-19 pandemic, overall surgical capacity within the hospitals was limited and many elective surgeries were postponed.9 Contrary to expectations, the current study shows a reduction in median time between diagnosis and initial treatment. A possible explanation is the decrease in number of (colorectal) cancer diagnoses during the COVID-19 pandemic.7 Besides the fact that the number of colorectal cancer diagnoses decreased during
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**Figure 1B**  Average number of rectal cancer patients of all ages treated per week, per tumor stage and per type of initial treatment.

![Rectal cancer stage I](image)

Period A, week 2-8 of 2020; Period B, week 9-11 of 2020; Period C, week 12-17 of 2020; Period D, week 18-26 of 2020.

**Table 2a**  Number of Colon Cancer Patients who Underwent (Acute) Resection, Adjuvant Therapy, or Stoma per Period.

|                  | Period A | Period B | P-Value | Period C | P-Value | Period D | P-Value | Period B-D | P-Value |
|------------------|----------|----------|---------|----------|---------|----------|---------|------------|---------|
| Patients         |          |          |         |          |         |          |         |            |         |
| N (%)            | 174      | 68       | .10     | 84       | .50     | 77       | .34     | 292        | .17     |
| Resection        | All      | 105 (60.3) | 33 (48.5) | 1.0 | 47 (56.0) | .50 | 77 (55.0) | .34 | 157 (53.8) | .17 |
| Period A         |          |          |         |          |         |          |         |            |         |
| Period B         |          |          |         |          |         |          |         |            |         |
| Period C         |          |          |         |          |         |          |         |            |         |
| Period D         |          |          |         |          |         |          |         |            |         |
| Period B-D       |          |          |         |          |         |          |         |            |         |
| Patients         |          |          |         |          |         |          |         |            |         |
| N (%)            | 77 (44.3) | 27 (39.7) | .52 | 38 (45.2) | .88 | 66 (47.1) | .61 | 131 (44.9) | .90 |

Period A, weeks 2 to 8 of 2020; Period B, weeks 9 to 11 of 2020; Period C, weeks 12 to 17 of 2020; Period D, weeks 18 to 26 of 2020; Period B to D, weeks 9 to 26 of 2020.

The P-value was calculated excluding missing values, using the Chi-squared test to compare patients diagnosed in period B, C, or D of 2020 with patients diagnosed in period A of 2020.

* Patients who received adjuvant therapy are divided in 4 periods based on surgery date, while the patients who underwent a resection are divided in 4 periods based on incidence date. Therefore, the proportions shown for adjuvant therapy are not calculated as a proportion of the total number of patients who underwent a resection shown in this table.

**Table 2b**  Number of Rectal Cancer Patients who Underwent (Acute) Resection, Neoadjuvant Therapy, or Stoma per Period.

|                  | Period A | Period B | P-Value | Period C | P-Value | Period D | P-Value | Period B-D | P-Value |
|------------------|----------|----------|---------|----------|---------|----------|---------|------------|---------|
| Patients         |          |          |         |          |         |          |         |            |         |
| N (%)            | 174      | 68       | .10     | 84       | .50     | 77       | .34     | 292        | .17     |
| Resection        | All      | 105 (60.3) | 33 (48.5) | 1.0 | 47 (56.0) | .50 | 77 (55.0) | .34 | 157 (53.8) | .17 |
| Period A         |          |          |         |          |         |          |         |            |         |
| Period B         |          |          |         |          |         |          |         |            |         |
| Period C         |          |          |         |          |         |          |         |            |         |
| Period D         |          |          |         |          |         |          |         |            |         |
| Period B-D       |          |          |         |          |         |          |         |            |         |
| Patients         |          |          |         |          |         |          |         |            |         |
| N (%)            | 77 (44.3) | 27 (39.7) | .52 | 38 (45.2) | .88 | 66 (47.1) | .61 | 131 (44.9) | .90 |

Period A, weeks 2 to 8 of 2020; Period B, weeks 9 to 11 of 2020; Period C, weeks 12 to 17 of 2020; Period D, weeks 18 to 26 of 2020; Period B to D, weeks 9 to 26 of 2020.

The P-value was calculated excluding missing values, using the Chi-squared test to compare patients diagnosed in period B, C, or D of 2020 with patients diagnosed in period A of 2020.
the COVID-19 pandemic, the number of cancer diagnoses in general also decreased, and many elective surgeries were postponed. In addition, colorectal cancer surgery generally does not require postoperative Intensive Care Unit (ICU) admission, which was the limiting factor in many hospitals. For this reason, cardiac and neurosurgery procedures were cancelled, which resulted in more capacity for elective colorectal cancer procedures. Although overall hospital capacity was limited, this did not impact the waiting time before surgery for colorectal cancer patients. This could be a possible explanation for the reduction in median time between diagnosis and initial treatment as found in the current study.

During the whole of the analyzed period, the region North/East of the Netherlands showed a significant decrease in the interval between diagnosis and initial treatment for colon patients. This region was in the beginning of the COVID-19 pandemic least affected by COVID-19, illustrating that even in small countries regional difference in cancer care can be observed in relation to infection rates.

We could observe changes in the median times between (neo)adjuvant therapy and surgery during the COVID-19 pandemic. The changes partly reflect the recommended measures to postpone surgery after adjuvant therapy and to postpone adjuvant therapy after surgery. However, there is also an increase trend towards longer waiting times after neoadjuvant therapy with further delaying surgery to increase the clinical response rate and enable better selection of patients with clinical complete response who are candidate for organ preserving treatment. Therefore, the change in median time does not necessarily have to be COVID-19 related. Due to the low number of patients, these results were not significant.

Results of our study show that the proportion of patients who received a stoma increased significantly during the COVID-19 period. This is likely related to a change in patient characteristics with a relative increase of symptomatic patients that presented in an emergency setting during the COVID-19 pandemic. Furthermore, not constructing an anastomosis or performing a defunctioning stoma lowers the risks of postoperative infectious complications such as wound infection or anastomotic leakage. Such a risk averse strategy is intended to lower the need for ICU admission. As the ICU was almost entirely occupied by COVID-patients, a colostomy may have been performed more often to reduce the need for additional ICU-beds.

For rectal cancer patients, a recommended measure published during the COVID-19 pandemic was to replace neoadjuvant chemoradiation with short course neoadjuvant radiotherapy and a long waiting time before a resection. Another recommended measure was to omit neoadjuvant radiotherapy if there was capacity available to perform surgery on short-term notice, because operative capacity was often difficult to estimate beyond the coming week. However, results of our study showed no significant differences in the use of neoadjuvant chemoradiation and neoadjuvant radiotherapy. Therefore, these recommended measures during the COVID-19 pandemic were apparently not implemented in clinical practice.

To our knowledge, this was the first study to report on the impact of the COVID-19 pandemic on colorectal cancer care on a population-based level. However, we could include data from 25 of the 70 hospitals in the Netherlands. Although this data will provide a good representation of the total colorectal cancer population in the Netherlands, the impact of data fluctuations unrelated to the COVID-19 pandemic cannot be excluded and interpretations of the results need to be made with caution.

**Conclusion**

Despite the disruptive impact of the COVID-19 pandemic on global health care, the impact on colorectal cancer care in the Netherlands was found to be limited. Only slight changes in colorectal cancer care during the COVID-19 pandemic were revealed, which was partly due to a higher proportion of symptomatic patients during the pandemic. Future studies will investigate the long-term effects of the COVID-pandemic on the outcome of these patients.

**Clinical Practice Points**

- To our knowledge, this was the first study to report on the impact of the COVID-19 pandemic on colorectal cancer care on a population-based level. Although this data will provide a good representation of the total colorectal cancer population in the Netherlands, the impact of data fluctuations unrelated to the COVID-19 pandemic cannot be excluded and interpretations of the results need to be made with caution.
- Despite the disruptive impact of the COVID-19 pandemic on global health care, the impact on colorectal cancer care in the Netherlands was found to be limited. Only slight changes in colorectal cancer care during the COVID-19 pandemic were shown, which was partly due to a higher proportion of symptomatic patients during the pandemic.
- First, the patient population changed during the COVID-19 pandemic because of the temporary halt of the colorectal cancer screening program and the recommendation of the Dutch authorities to only visit the GP with serious complaints resulting in several changes in type of first treatment.
- Second, colorectal cancer patients experienced no delay in start of first treatment after diagnosis. The interval became shorter since the decrease in number of cancer diagnosis and the decrease in elective surgeries during the COVID-19 pandemic.
- Last, the proportion of patients who received a stoma during the COVID-19 pandemic was higher.
- Future studies will investigate the long-term effects of the COVID-pandemic on the outcome of these patients.

**Disclosure**

The authors have stated that they have no conflicts of interest.

**Supplementary materials**

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.clcc.2022.02.005.

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