



A Follow-up Report on the Diagnosis of Gastrointestinal Cancer during the COVID-19 Pandemic in Akita Prefecture, Japan in 2021

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We recently reported the decrease in the number of gastrointestinal (GI) cancer diagnoses in 2020 due to disturbance of the healthcare system by the coronavirus disease 2019 (COVID-19) pandemic, using a hospital-based cancer registration system in Akita prefecture, Japan. In this study, we extended the research by showing the latest data (2021) on the number of cancers and examinations. Information on the occurrence and stage of esophageal, gastric, and colorectal cancers was collected from the same database. The number of GI examinations (cancer screening procedures and endoscopic examinations) was also investigated. Following the immediate decrease in the numbers of both GI examinations and GI cancer diagnoses in 2020, a rebound increase in the numbers of GI cancer diagnoses—especially colorectal cancers—was observed in 2021, resulting from an increased number of GI examinations i.e., the total number of colorectal cancers in 2021 increased by 9.0% and 6.8% in comparison to 2020 and pre-pandemic era, respectively. However, the rebound increase in 2021 was largely due to an increase in early-stage cancers, and there was no apparent trend toward the increased predominance of more advanced cancers. It therefore seems that we managed to escape from the worst-case scenario of disturbance of the healthcare system due to pandemic (i.e., an increase in the number of more advanced cancers due to delayed diagnoses). We need to continue to watch the trends in Akita prefecture, which has the highest rate of mortality from the 3 major GI cancers in Japan.

Keywords: cancer screening; cancer stage; colorectal cancers; COVID-19 pandemic; gastrointestinal cancers

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Introduction

Coronavirus disease 2019 (COVID-19) was first identified in Wuhan, China in December 2019, and subsequently spread worldwide in 2020. The pandemic placed a serious burden on the overall healthcare system, not only the resources used directly in the treatment of COVID-19, but also those used for other serious life-threatening diseases, such as cancer. Indeed, previous studies have repeatedly shown that the COVID-19 pandemic led to a substantial decrease in diagnosed gastrointestinal (GI) cancers in parallel with a decreased number of diagnostic procedures (e.g., endoscopy) (Dinmohamed et al. 2020; Khan et al. 2021; Rutter et al. 2021). In addition, some studies have shown an *increase* in the number of advanced GI cancers even at a time when the total number decreased, due to delayed cancer diagnoses in 2020 (Lui et al. 2020; Kuzuu et al. 2021). Intriguingly, recent results from a simulation model revealed a sharp decrease in the number of diagnosed cancers during the pandemic, followed by a projected increase in the future cancer diagnoses (Ward et al. 2021). In that report, compared with no COVID-19 scenario, estimated number of total cancers decreased by 32% in 2020, followed by 14% increase in 2021 and 10% increase in 2022, in which the increase is mainly due to advanced stage cancers (Ward et al. 2021). However, although these studies warned about the possibility of a rebound increase in the number of cancer diagnoses, especially advanced-stage cases in the months and years to come, most demonstrated that the disturbance only had a short-term influence on the diagnosis of GI cancers within the first year of the pandemic (2020) (Dinmohamed et al. 2020; Lui et al. 2020; Khan et al. 2021; Rutter et al. 2021; Kuzuu et al. 2021), and, as far as we know, few studies have demonstrated the subsequent trends.

Similarly, a nationwide survey in Japan recently reported that the numbers of GI cancer diagnoses decreased in 2020 due to the COVID-19 pandemic (Okuyama et al. 2022), although the subsequent trends are yet to be shown. We recently reported that the number of GI cancers decreased in 2020, concomitant with the decreased number of cancer screening procedures and diagnostic endoscopy procedures, in a population-based study that was conducted in Akita prefecture, located in the northern Japan (Iijima et al. 2022). Importantly, in that study, we also found an *increase* in the number of stage IV (the most advanced stage) esophagogastric cancers (EGCs) in 2020 (Iijima et al. 2022); hence, the subsequent, latest trend in GI cancer diagnoses in the area is noteworthy. In the present study, we have extended our recent population-based study by showing the latest data (2021) on the number of GI cancers and GI examinations (GI cancer screening procedures and endoscopic examinations) during the ongoing pandemic.

Materials and Methods

In the preceding study, we presented the number of GI

cancers in Akita prefecture from 2016 to 2020 (Iijima et al. 2022). In the present follow-up study, we further collected additional data on the same matrix in 2021. Regarding the occurrence and stage of GI cancers, we employed the database from the collaborative Akita prefecture hospital-based registration system for cancers (Koizumi et al. 2018a, b), in which all 11 cancer care hospitals (designated by the Ministry of Health, Labour and Welfare in Japan) located in Akita prefecture participated. Overall, these 11 hospitals cover 81.0% of cancer treatments in the prefecture (National Cancer Center Japan: https://www.ncc.go.jp/jp/information/pr_release/2021/1126/index.html). Information on the initial treatment for cancers was also collected in the current study. As a reference, we also collected the date on hepato-biliary-pancreatic cancers using the same registration system during the same period. In addition, data on the number of esophagogastroduodenoscopy (EGD) and colonoscopy (CS) procedures performed at the 11 cancer care hospitals were collected.

Regarding the number of GI cancer screening procedures (upper GI series with barium meal and fecal occult blood test), we collected data for the three consecutive years from 2019 to 2021 from two exclusive institutes that manage cancer screening procedures in Akita prefecture (Akita Foundation for Healthcare, and The Akita Prefectural Federation of Agricultural Cooperatives for Health and Welfare). Note that biannual endoscopic screening for gastric cancers in place of annual radiological screening started in parallel in Akita prefecture in 2021. Hence, a small portion (< 1,000) of patients undergoing screening selected endoscopic screening in 2021, at their discretion.

The data from 2021 (the second year of the COVID-19 pandemic) were compared with the average data of the previous four years (2016-2019) (the pre-pandemic era) and 2020 (the first year of the pandemic). Similar to our preceding paper (Iijima et al. 2022), the occurrence of esophageal and gastric cancers was combined as EGC, as both cancers are detected by the same GI examinations. Similarly, because the number of stage II and III cases for each cancer was relatively small, these were summed for stage-specific comparisons (Iijima et al. 2022). The temporal changes in the number of cancer diagnoses and examinations were expressed as the % change from the previous year. This analysis was approved by the Akita University School of Medicine Ethics Committee (2796). The subject age was expressed as the mean and standard deviation (SD), and compared using Student's t-test. Sex was expressed as the number and proportion, and compared using the chi-square test. P values of < 0.05 were considered statistically significant.

Results

For each site of neoplasia, the mean age at the diagnosis and the sex ratio are shown in Table 1 depending on the calendar year. Almost all these neoplasia (more than 97%) were cancers, and further analyses were performed using

Table 1. The mean age at the diagnosis and the sex ratio for each site of neoplasia before and during COVID-19 pandemic.

Sites of neoplasia	Age, years, mean (SD)			Sex, male/female, n (%)		
	2016-2019	2020	2021	2016-2019	2020	2021
Esophagus	71.6 (9.1)	73.4 (9.1)**	72.7 (9.3)	1,036 (87.1) / 153 (12.9)	245 (86.6) / 30 (13.4)	234 (84.5) / 43 (15.5)
Stomach	73.3 (10.3)	74.5 (10.1)**	74.5 (10.2)**	3,582 (68.9) / 1,617 (31.1)	784 (67.9) / 370 (32.1)	830 (70.9) / 341 (29.1)
Colorectum	71.1 (11.5)	71.9 (11.4)*	71.7 (11.7)	3,983 (60.5) / 2,597 (39.5)	998 (61.9) / 613 (38.1)	1,057 (60.4) / 693 (39.6)
Liver-bile duct-pancreas	75.3 (10.5)	76.3 (11.2)*	74.4 (11.0)#	1,607 (58.3) / 1,151 (41.7)	437 (57.5) / 323 (42.5)	181 (53.9) / 155 (46.1)

*p < 0.05, **p < 0.01 compared with values of 2016-2019.

#p < 0.05 compared with values of 2020.

Otherwise, not significant.

data of cancers alone.

Occurrence of GI cancers

The total number of EGCs slightly increased by 1.5% from 1,396 in 2020 to 1,417 in 2021; however, the number in 2021 was still 9.7% lower in comparison to that in the pre-pandemic era (n = 1,569) (Fig. 1A). Regarding stage-specific comparisons, the number of stage II/III EGCs increased by 27.3% from 238 in 2020 to 303 in 2021, while the number of stage I and IV decreased from 801 and 290 to 785 and 264, respectively. In any case, the number of any-stage EGC cases in 2021 was decreased in comparison to the pre-pandemic era. The proportion of stage II/III EGCs decreased and that of stage IV EGCs increased in 2020 in comparison to the pre-pandemic era, but the changes seemed to be transient and the proportions of each stage of EGC in 2021 became more like the proportions in the pre-pandemic era (Fig. 2A).

The total number of colorectal cancers (CRCs) was 1,726 in 2021, and increased by 9.0% from 1,585 in 2020 and by 6.8% from the pre-pandemic era (n = 1,616) (Fig. 1B). Stage-specific comparisons of CRCs revealed that the number of stage 0/I CRCs prominently increased by 15.2% from 742 in 2020, and by 9.2% from 783 in the pre-pandemic era, to 855 in 2021. In addition, the numbers of both stage II/III and IV CRCs only marginally increased in 2021 in comparison to the numbers in 2020 and in the pre-pandemic era. The distribution of the stage in CRCs showed that the proportions of each stage were largely similar among the 3 time periods (pre-pandemic, 2020, and 2021) (Fig. 2B). Temporal trends in the proportions of initial treatments for EGCs and CRCs are shown in Fig. 3, and there was no pandemic-related change for them.

The number of hepato-biliary-pancreatic cancers, which are generally detected on the appearance of symptoms, such as abdominal pain, jaundice, weight loss, not on the screening examination, steadily increased during the study period irrespective of COVID-19 pandemic (Fig. 1C).

GI screening procedures

Following the initial 30.3% and 29.1% decrease in the number of upper GI series and fecal occult blood tests, respectively, in the first year of the pandemic (2020) in comparison to those in 2019, these numbers partially recov-

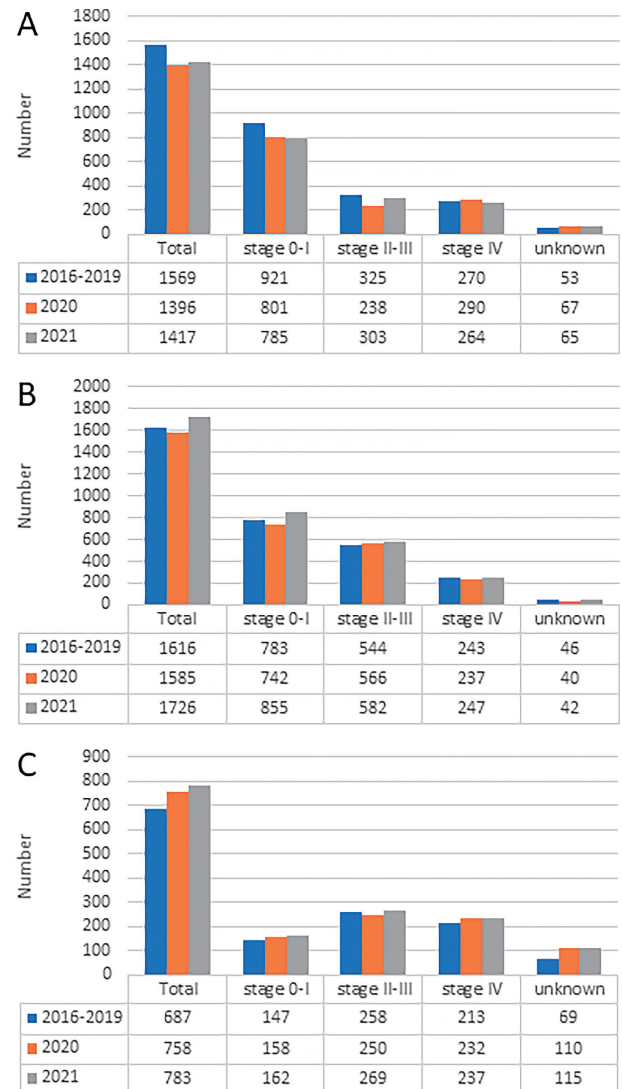


Fig. 1. Temporal trends in the numbers of esophagogastric cancer (A), colorectal cancer (B), and hepato-biliary-pancreatic cancer (C) cases according to the cancer stage in Akita prefecture.

ered in the second year of the pandemic (2021) (Fig. 4). That is, the number of upper GI series increased by 25% in 2021 (n = 55,823) in comparison to 2020 (n = 44,670), but it was still 13% lower than that in 2019 (n = 64,055) (Fig. 4A). Similarly, the number of fecal occult blood tests

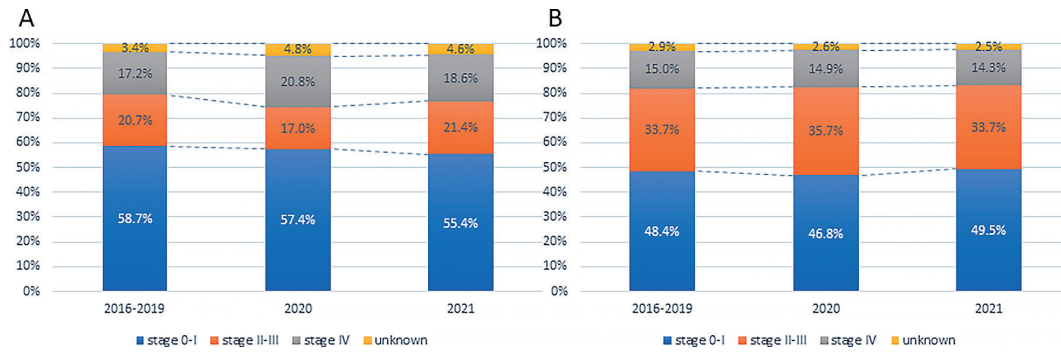


Fig. 2. Temporal trends in the proportions of each cancer stage for esophagogastric cancer (A) and colorectal cancer (B) in Akita prefecture.

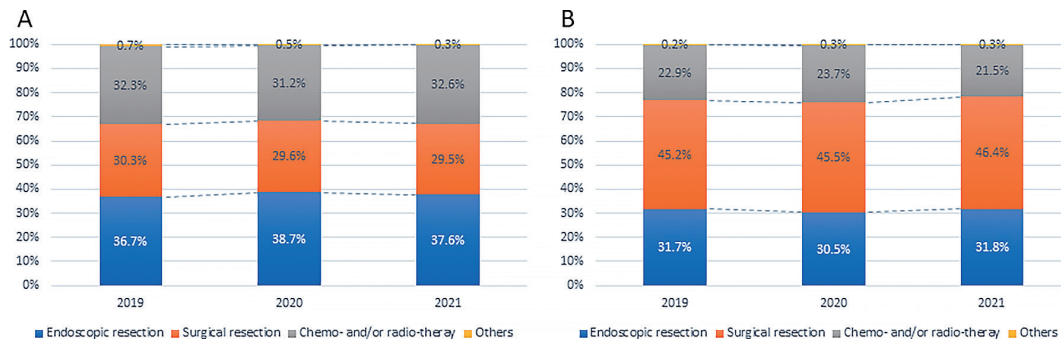


Fig. 3. Temporal trends in the proportions of initial treatments for esophagogastric cancer (A) and colorectal cancer (B) in Akita prefecture.

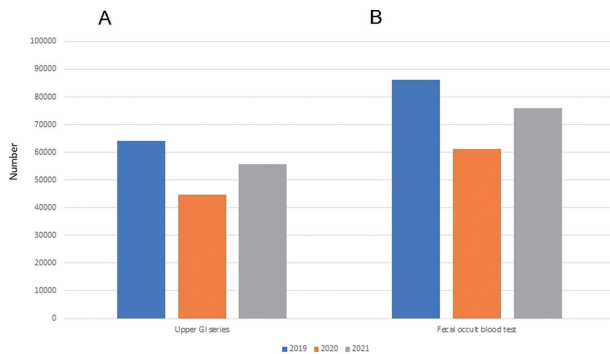


Fig. 4. Temporal trends in the number of cancer screening procedures in Akita prefecture. A: Upper GI series with barium meal. B: Fecal occult blood test.

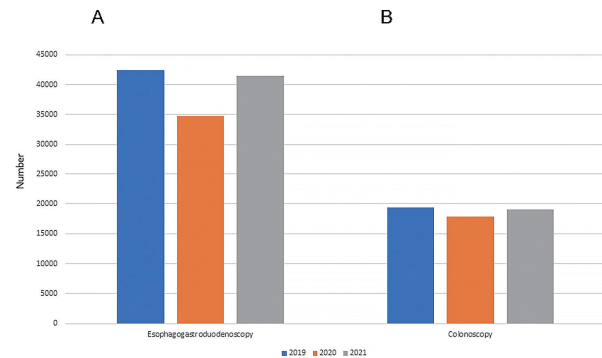


Fig. 5. Temporal trends in the number of esophagogastrroduodenoscopy (A) and colonoscopy (B) procedures performed at the 11 cancer care hospitals in Akita prefecture.

increased by 24% from 61,099 in 2020 to 75,870 in 2021, although the number in 2021 was still 12% lower than that in 2019 ($n = 86,181$) (Fig. 4B).

GI endoscopic examinations

The degrees of reduction in the number of endoscopic examinations in 2020 in relative to 2019 were relatively smaller in comparison to those observed in GI screening procedures as shown above, and the numbers seemed nearly fully recovered in 2021 (Fig. 5). Although the number of EGD procedures decreased by 18.0% from 42,433 in 2019 to 34,793 in 2020, it increased to 40,281 in 2021, which

was a similar level to that in 2019 (Fig. 5A). Similarly, the number of CS procedures decreased by 7.8% from 19,362 in 2019 to 17,844 in 2020, and increased to 18,351 in 2021 (Fig. 5B).

Discussion

Using a reliable hospital-based registration system in Akita prefecture, which covers 81% of the GI cancers that occur in our area (Koizumi et al. 2018a, b; National Cancer Center Japan: https://www.ncc.go.jp/jp/information/pr_release/2021/1126/index.html), we have recently reported that the number of GI cancer diagnoses decreased due to

the disturbance of the healthcare system during the COVID-19 pandemic in 2020 (Iijima et al. 2022). The present study is a follow-up report using the same database, which investigates the influence of the disturbance of the healthcare system in our area up to the second year of the pandemic (2021). Following the immediate decrease in numbers of both GI examinations and GI cancer diagnoses in the first year (2020) of the pandemic, we found a rebound increase in the numbers of diagnosed GI cancers, especially for CRCs in the second year (2021), probably resulting from the increased number of GI examinations that were performed in the year. However, based on the additional data of 2021, the rebound increase in the number of CRCs in 2021 was found to be due largely to an increase in early-stage cancers, and there was no apparent trend toward the increased predominance of more advanced GI cancers.

The numbers of both GI cancer screening procedures and endoscopic examinations were decreased in Akita prefecture in 2020. This was responsible for the decreased number of GI cancer diagnoses in the area. Here, we found a substantial, rebound increase in the number of these GI examinations in our area in 2021. Nonetheless, it was also revealed that the decrease in the number of cancer screening procedures in 2020 was greater than the decrease in the number of endoscopic examinations. In contrast, in 2021, the number of cancer screening procedures had only partially recovered, while the number of endoscopic examinations had nearly fully recovered. The partial recovery in cancer screening procedures that was observed in our area is consistent with a recent preliminary report based on a nationwide survey in Japan (Japan Cancer Society: <https://www.jcancer.jp/news/12832#:~:text=2021>). In order to prevent the spread of COVID-19 infection, measures were taken in cancer screening procedures, such as limiting the number of people undergoing examinations at the examination venue each day and shifting from group examinations to individual examinations (Japan Cancer Society: <https://www.jcancer.jp/news/12832#:~:text=2021>), which would be responsible for the partial recovery in the number of GI cancer screening procedures in 2021.

Accordingly, as expected, the increase in the number of GI examinations in 2021 led to a concomitant increase in the total number of GI cancer diagnoses, especially for CRCs, in Akita prefecture in the same year. In addition, the increase in the total number of CRCs in 2021 largely resulted from the increase in early stage (stage 0/I) CRC. The smaller extent of increase in the total number of EGCs in 2021, relative to CRC, may be due partly to the natural temporal declining trend in gastric and esophageal cancer relative to CRC in Japan (National Cancer Center Japan: <https://ganjoho.jp/public/index.html>), as shown in the current study, e.g., esophageal cancer: $n = 297$ (average of 2016-2019), 281 (2020), and 275 (2021); gastric cancer: $n = 1,272$ (average of 2016-2019), 1,115 (2020), and 1,142 (2021). The natural temporal decreasing trend in gastric and esophageal cancer could also be responsible for some-

what different trends of stage 0/I cancers between EGCs and CRCs in 2021, e.g., stage 0/I cancers slightly decreased for EGCs, but increased for CRCs.

The delayed diagnosis of GI cancers due to the pandemic could ultimately lead to an excess of advanced cancers and death in the coming years (Dinmohamed et al. 2020). Indeed, in our recent study in Akita prefecture, such signs may have already appeared within the first year of the pandemic (2020), that is, we found a 7.2% increase in the number of the stage IV EGCs in 2020 in comparison to the pre-pandemic era (Iijima et al. 2022). Furthermore, a recent simulation model study from Chile predicted a worse-case scenario (i.e., an increase in the number of advanced cancers) would emerge in during the second year of the pandemic (Ward et al. 2021), which made us interested in the data from our area in 2021. Nonetheless, the current study did not find a further increase in the number of stage IV EGCs in terms of either the number or the proportion among total cancer cases in 2021. In addition, regarding CRCs, we found that the numbers of stage II/III and stage IV cases were only slightly increased in comparison to that in 2020 although the proportion of each stage of CRC was largely similar, irrespective of the pandemic. Thus, at present, the worst-case scenario resulting from the delay in cancer diagnoses due to the COVID-19 pandemic seems to have been avoided in Akita prefecture.

We need to wait for the latest reports on the occurrence of GI cancers from other countries, where the worse-case scenario was predicted for 2021 (Ward et al. 2021). Nonetheless, it is possible that the ultimate impact resulting from the disruption of the healthcare system may be relatively small in Japan in comparison to other countries, although we still need to carefully watch the subsequent trends in our area in the coming years. There are several possible explanations for the discrepancy. First, the number of infected subjects and deaths in Japan were much lower in comparison to other countries, especially in the initial phase of the pandemic. Accordingly, the execution of GI examinations fully resumed within 1-3 months after the start of the pandemic, and it has not been restricted since then (Irisawa et al. 2020). In addition, the development and widespread use of various infection protection devices for endoscopy such as mouthpieces, facial masks, and face shields to prevent droplet dispersal may also have contributed to maintaining the number of endoscopy during the ongoing pandemic in Japan (Endo et al. 2020; Onoyama et al. 2020; Hikichi et al. 2022). Second, GI examinations, in particular, endoscopic examinations, have long been prevalent in Japan. Hence, short-term interruption of GI examinations by the pandemic may have had only a small influence on the accumulating beneficial effects that had been yielded by periodic examinations in Japan.

The strength of this study is that it was a population-based survey on the latest trends in GI examinations and accompanying GI cancer diagnoses in Akita prefecture, Japan. A population-based study in a defined area is essen-

tial to know the changes in the number and stage distribution of cancers diagnosed before and after the pandemic, since the capacity of an individual hospital to see cancer patients may have changed due to how medical resources are directed as a result of the pandemic (Iijima et al. 2022; Kajiwar Saito et al. 2022; Kodama et al. 2023). Here, we successfully revealed the latest trend in GI cancer diagnoses in Akita prefecture in 2021. Although a very recent preliminary nationwide survey has recently reported the latest (2021) trends in the occurrence of GI cancers in Japan (National Cancer Center Japan: https://www.ncc.go.jp/jp/information/pr_release/2022/1209/index.html), the current report from Akita prefecture is still valuable because it is a report from the area that would be most severely affected by the pandemic, considering that the mortality rates associated with the three major GI cancers in this area (e.g., esophageal cancer, gastric cancer, and CRC) have always been the highest in Japan (National Cancer Center Japan: <https://ganjoho.jp/public/index.html>). In addition, the investigation of both the occurrence of GI cancers and GI examinations in a given area enables us to comprehensively understand the potential causal relationship between the two observations.

On the other hand, one limitation of this study is that we could not count the total number of endoscopic examinations performed in our area, hence we substituted the number performed in 11 cancer care hospitals for the total numbers in this study. A comprehensive survey on the total number of endoscopic examinations before and during the pandemic in a given area is warranted.

In conclusion, using the latest database of the hospital-based registration system in Akita prefecture, we found a rebound increase in the total number of CRCs in 2021 due to a compensatory increase in GI examinations. However, the increase predominantly results from an increase in cases of early-stage cancer. Hence, with regard to the consequences of the disturbance of healthcare system due to pandemic, we have—thus far—managed to escape from the worst-case scenario (i.e., an increase in more advanced cancers due to delayed diagnoses). We still need to watch the further trends in the occurrence of GI cancers in Akita prefecture, the area with the highest mortality from the 3 major GI cancers in Japan.

Conflict of Interest

The authors declare no conflict of interest.

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