



A Final Report on the Real Impact of the COVID-19 Pandemic on the Diagnosis of Gastrointestinal Cancer in Akita Prefecture, Japan in 2022

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The long-term impact of the coronavirus disease 2019 (COVID-19) pandemic on the disruption of gastrointestinal cancer diagnoses remains unclear. This study investigated the actual impact on esophagogastric cancer (EGC) and colorectal cancer (CRC) diagnoses up to the third year of the pandemic in Akita Prefecture, Japan, using population-based registry data. We collected data on the annual number of EGC and CRC diagnoses using a database from the collaborative Akita Prefecture hospital-based registration. The net number of cancers diagnosed in the first three years of the pandemic (2020-2022) were compared with those diagnosed in the three years before the pandemic (2017-2019). Changes in the proportion of cancer stage and initial treatment for diagnosed EGC and CRC after the pandemic were then compared. The total number of EGCs was 9.3% lower in the first three years of the pandemic than in the three years before, probably due to its long-term declining trend. The total number of CRCs in the first three years of the pandemic exceeded that in the three years before, suggesting successful recovery of the diagnostic procedure. The proportion of cancer stages and initial treatment for EGCs and CRCs remained largely unchanged after the onset of the pandemic. Based on the population-based registry data from the first three years of the pandemic, the disruption of gastrointestinal cancer diagnoses caused by the pandemic is settling down without any substantial disease progression, even in Akita Prefecture, the area with the highest incidence of cancer in all of Japan.

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

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic has disrupted clinical practice, including cancer diagnoses. This led to a substantial decrease in number of diagnosed cancers worldwide in 2020, the first year of the COVID-19 pandemic (Lui et al. 2020; Rutter et al. 2021; Doeve et al. 2023). In addition, the reduction of diagnoses has occurred mainly in the early stages of cancer (Han et al. 2023; Schafer et al. 2024), a trend that is more prominently

observed in screening-detectable cancers, such as colorectal cancer (CRC), due to decreases in screening prevalence to lower the burden of non-emergency healthcare (Han et al. 2023; Schafer et al. 2024).

The observation that many cancers went undiagnosed in the first year of the pandemic (2020) may eventually result in a significant stage shift towards the increased detection of more advanced-stage cancers (e.g., a larger proportion of patients diagnosed at advanced stages) in the coming years (Maida 2020; Dinmohamed et al. 2020; Iijima

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et al. 2024). Indeed, some simulation model studies consistently predicted that the increased cancer mortality resulting from delayed diagnoses would last over a period of several years (Maringe et al. 2020; Ricciardiello et al. 2021; Ward et al. 2021; Malagón et al. 2022). Indeed, some studies have already demonstrated a potential stage shift of diagnosed cancers in 2020 (Lui et al. 2020; Kuzuu et al. 2021).

Several subsequent studies have reported the real impact of the pandemic on cancer diagnoses in the second year (2021) (Englum et al. 2023; de Sousa et al. 2023; Garrido-Cantero et al. 2023; Toes-Zoutendijk et al. 2023; Suh et al. 2023), showing somewhat conflicting results; some reported a worse scenario in 2021 than in previous years (e.g., the number of diagnosed cancers remained low and/or there was a significant stage shift towards more advanced stages) (Englum et al. 2023; de Sousa et al. 2023; Garrido-Cantero et al. 2023), while others reported a nearly full recovery in 2021 (e.g., the number recovered to the pre-pandemic level) without any shift in the stage of the diagnosed cancers (Toes-Zoutendijk et al. 2023; Suh et al. 2023). Since some of the above simulations predicted that the worst scenario (e.g., the highest excess cancer mortality) would appear in the third year of the pandemic (2022) (Maringe et al. 2020; Ward et al. 2021; Malagón et al. 2022), further longer-term follow-up studies are required to determine the ultimate impact of the pandemic on cancer diagnoses. However, to our knowledge, there have been few reports on the impact three years into this pandemic.

We also reported the real impact of the pandemic on the diagnosis of detectable gastrointestinal (GI) cancers, such as esophageal cancers (ECs), gastric cancers (GCs), and CRCs, up to two years after the pandemic had begun, in a population-based survey in Akita Prefecture, Japan (Iijima et al. 2022, 2023b). In these reports, following the immediate decrease in the number of GI cancer diagnoses in the first year (2020) of the pandemic, we found a rebound increase in the number of diagnosed GI cancers mainly for those at early stages in the second year (2021), at which point there was no apparent trend toward the increased predominance of more advanced GI cancers (Iijima et al. 2022, 2023b). Considering that the area in question, Akita Prefecture, should have experienced the worst effects of the pandemic in Japan due to it having the highest incidence and mortality of GI cancers in the country (Koizumi et al. 2018a, b), our observations of the latest trends in GI cancer diagnoses in Akita Prefecture are considered noteworthy.

In the present study, we extended our recent population-based survey by showing the data up to the third year (2022) of the pandemic to estimate its ultimate impact on GI cancer diagnoses.

Material and Methods

In previous studies (Iijima et al. 2022, 2023b), we presented the clinical features of GI cancers diagnosed from 2016 to 2021 in Akita Prefecture, Japan. In the present study, we collected additional data for 2022 from the same

database. In this analysis, we employed a database from the collaborative Akita Prefecture hospital-based registration system of cancers, in which all 11 cancer care hospitals, designated by the Ministry of Health, Labour and Welfare in Japan, located in Akita Prefecture participated (Koizumi et al. 2018a, b). Overall, these 11 hospitals cover 80%-90% of the treatments for cancers occurring in the prefecture (Koizumi et al. 2018a, b). Using this registration system, we present data on the annual number of GI cancers diagnosed by cancer stage and initial treatment. As a reference, we also collected data on diagnoses of hepato-biliary-pancreatic (HBP) cancers using the same registration system during the same period, as these cancers are generally detected on the appearance of symptoms, such as abdominal pain, jaundice, and weight loss, and not on screening examinations. Data on age and sex were collected for each cancer case.

The annual data from the first, second, and third years (2020, 2021, and 2022) of the pandemic were compared with those of the average of the previous four-year 2016-2019 (pre-pandemic era), in a similar fashion to our preceding studies (Iijima et al. 2022, 2023b). The temporal changes in the number of cancers and examinations were expressed as a percentage change of the previous year. The net numbers of GI cancers diagnosed in the first three years of the pandemic (2020-2022) were then compared with those in the three years before the pandemic (2017-2019) to examine recovery phase for identifying cancers that went undiagnosed in the initial phase of the pandemic. In the analyses, similar to our previous paper (Iijima et al. 2022, 2023b), clinical data on ECs and GCs were combined as esophagogastric cancers (EGCs), as both cancers were detected by the same GI examinations. Similarly, because the number of stage II and III cases for each cancer was relatively small, they were summed for stage-specific comparisons (Iijima et al. 2022, 2023b). Each subject's age was expressed as the mean and standard deviation (SD) and compared using Student's *t*-test, and sex was expressed as the number and proportion and compared using the chi-square test. Statistical significance was set at $P < 0.05$.

This study was approved by the Akita University School of Medicine Ethics Committee (No.2796).

Results

The mean age and sex ratio of patients with each digestive neoplasia registered in our registration system during the study period are chronologically shown in Table 1. Of these neoplasms, the vast majority (> 98%) were cancers; hence, the following analyses were confined to cases with cancers.

GI cancers

The total number of EGCs showed a large drop (11.0%) in 2020 compared to the pre-pandemic value; after a small rebound increase in 2021, it showed a further decrease in 2022 (Fig. 1A). Overall, we found 453 (9.8%)

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	2020	2021	2022
Esophagus	71.6 (9.1)	73.4 (9.1)**	72.7 (9.3)	1,036 (87.1)/153 (12.9)	234 (84.5)/43 (15.5)	227 (85.3)/39 (14.7)
Stomach	73.3 (10.3)	74.5 (10.1)**	74.5 (10.2)**	3,582 (68.9)/1,617 (31.1)	830 (70.9)/341 (29.1)	731 (66.6)/367 (33.4)
Colorectum	71.1 (11.5)	71.9 (11.4)*	71.7 (11.7)	4,620 (72.3)/1,770 (27.7)	1,057 (60.4)/693 (39.6)	930 (57.6)/684 (42.4)
Hepato-biliary-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)	419 (56.2)/326 (43.8)

*p < 0.05, **p < 0.01 compared with values of 2016-2019. [#]p < 0.05 compared with values of 2020. Otherwise, not significant.

less diagnosed EGC cases in the first three years (2020-2022) of the pandemic than in the three years before the pandemic (2017-2019) (Fig. 1D). On the other hand, the total number of CRC cases slightly decreased in 2020, and after showing a prominent rebound in 2021, the numbers seem to return to the pre-pandemic baseline in 2022 (Fig. 1B). Of note, the total number of diagnosed CRC cases in the first three years (4,907 in 2020-2022) of the pandemic exceeded that in the previous three years (4,822 in 2017-2019) (Fig. 1D).

Regarding the change in the distribution of EGC stages, the number of early-stage (stage 0-I) EGC cases decreased considerably by 13.0% in 2020 and continued to stay at a lower level in 2021 and 2022 than before the pandemic. Meanwhile, there was no clear trend (at least no increasing trend) in the number of more advanced EGC cases (stages II-III or IV) after the pandemic (2020-2022) in comparison with each pre-pandemic baseline (Fig. 1A). Regarding the distribution of CRC stages, similar to the total number, the trends in early-stage (stage 0-I) CRC in 2022 returned to the pre-pandemic baseline after showing a rebound increase in 2021. Although the numbers of stage II or III CRC cases were numerically higher in the first three years of the pandemic than at the pre-pandemic baseline, there was no steady increasing trend during this three-year period. In addition, there was no clear trend (at least no increase) in the number of stage IV CRC cases (Fig. 1B).

The proportions of cancer stage and initial treatment for EGCs and CRCs are shown in Figs. 2 and 3, respectively. There was a slight fluctuation in the cancer stage proportions during the first three years of the pandemic; however, there was no steady temporal trend (at least, no obvious stage shift towards more advanced stages) during this three-year period for either cancer in comparison with the pre-pandemic baseline (Fig. 2). Meanwhile, the trends remained quite stable during the study period, and there were no obvious temporal changes in the initial treatment for either cancer (Fig. 3).

HBP cancers

The continuously increasing trend in the total number of HBP cancers observed in 2020 and 2021 subsided considerably by 2022. However, there seems to have been a steady increasing trend in the number of stage IV HBP cancers in the three-year period of 2020 to 2022 (Fig. 1C).

Discussion

To our knowledge, this is the first report to use population-based data on the impact of the COVID-19 pandemic on the diagnosis of GI cancers over a period of three years. We found that the disturbance of GI cancer care (diagnoses and treatment) yielded by the initial phase of the pandemic in 2020 seems to have settled down in the three years since the outbreak without any substantial disease progression.

In the first year of the COVID-19 pandemic, the number of diagnosed cancers decreased worldwide, mainly for

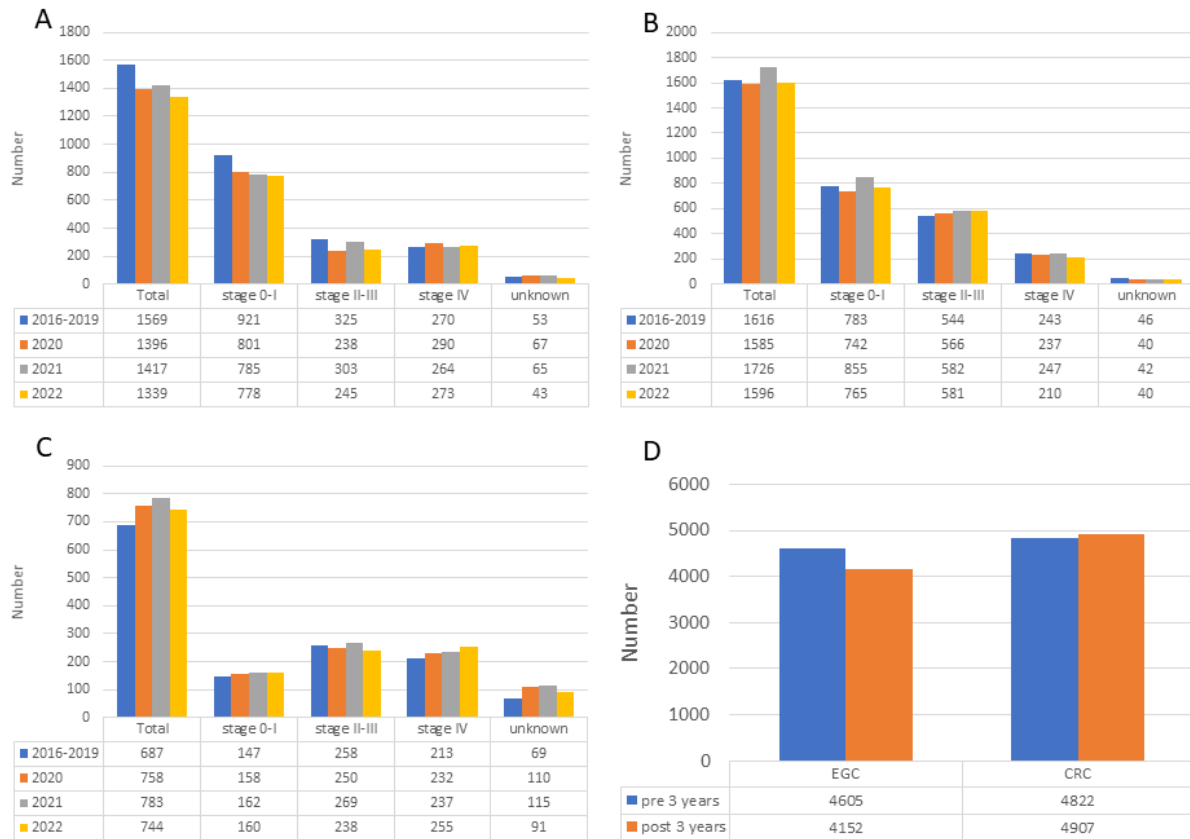


Fig. 1. Temporal trends from 2016 to 2022 in the numbers of esophago-gastric cancer (A), colorectal cancer (B), and hepato-biliary-pancreatic cancer (C) cases according to the cancer stage in Akita Prefecture. A comparison of the total number of esophago-gastric and colorectal cancer cases between the three years before the pandemic (2017-2019) and first three years (2020-2022) of the pandemic (D). EGC, esophago-gastric cancer; CRC, colorectal cancer.

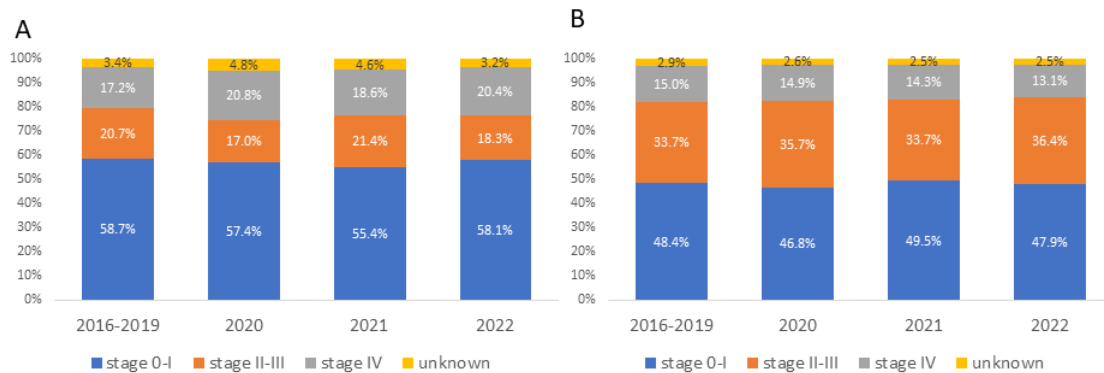


Fig. 2. Temporal trends from 2019 to 2022 in the proportions of each cancers stage for esophago-gastric cancer (A) and colorectal cancer (B) in Akita Prefecture.

early-stage cancers (Lui et al. 2020; Rutter et al. 2021; Doeve et al. 2023; Han et al. 2023; Schafer et al. 2024), which may have ultimately lead to an increase in the proportion of cancers detected in advanced stages in the coming years (Maida 2020; Dinmohamed et al. 2020; Iijima et al. 2024). However, the situation in the second year of the pandemic varied by country and region. A nationwide survey in the US revealed that overall cancer diagnoses,

including CRC, remained consistently below pre-COVID levels in 2021 (Englum et al. 2023). Furthermore, a preliminary report using national cancer registry data in Brazil revealed that there was a significant stage shift of cancers towards more advanced stages in 2020 and 2021 (de Sousa et al. 2023), and a similar trend was observed in Spain (Garrido-Cantero et al. 2023). In contrast, a nationwide survey in the Netherlands revealed that there was no sub-

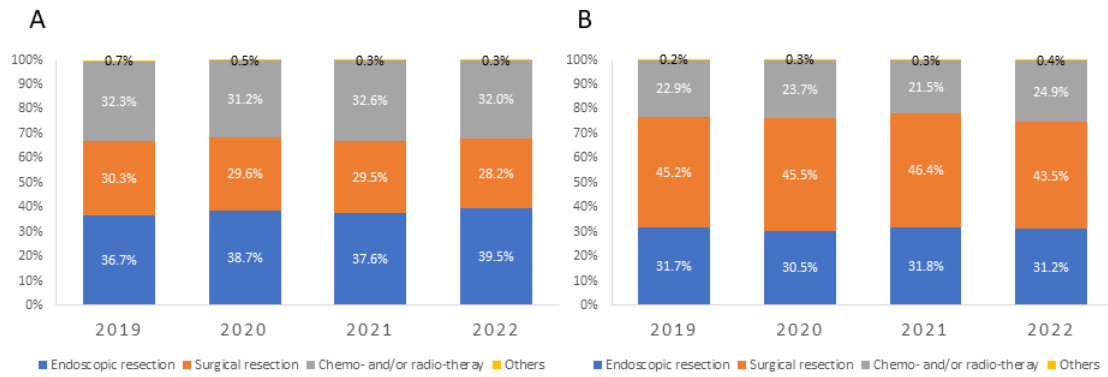


Fig. 3. Temporal trends from 2019 to 2022 in the proportions of initial treatments for esophago-gastric cancer (A) and colorectal cancer (B) in Akita Prefecture.

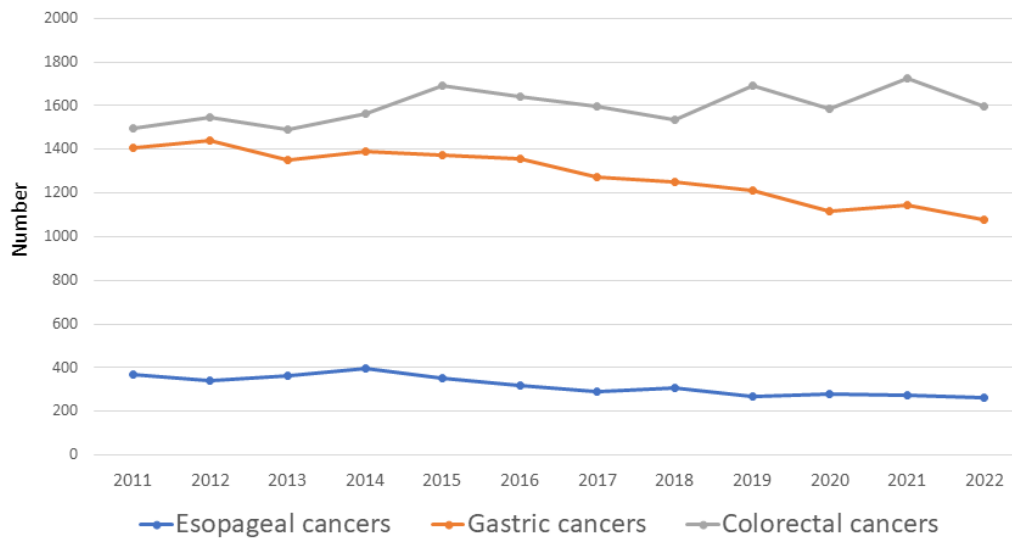


Fig. 4. Temporal trend in the annual total number of esophageal, gastric, and colorectal cancers since 2011 in Akita Prefecture.

stantial delay in CRC diagnosis in the Dutch screening program in 2021 (Toes-Zoutendijk et al. 2023). In addition, annual claims data from the National Health Insurance Program in Korea revealed that the number of diagnosed GCs had fully recovered by 2021 without any stage shift of cancers (Suh et al. 2023). Thus, different countries have been impacted differently by the pandemic, depending on the magnitude of the pandemic in a given country, the resulting disruption of their healthcare system, and the resilience of their healthcare system. In addition, disparities in access to healthcare systems by ethnicity or limited income within a country may also be responsible for the differing real impacts among countries and regions (Lofters et al. 2023; Negoita et al. 2024).

A recent nationwide survey in Japan reported a substantial decrease in the number of cancers diagnosed during the first year of the pandemic (2020) (Okuyama et al. 2022). Subsequently, a very recent preliminary survey in Japan reported nearly complete recovery of the number of diagnosed cancers at all sites in the second year of the pandemic

(2021), except for GCs, as in our study, compared with each pre-pandemic level (Ministry of Health, Labour and Welfare 2023). However, the report did not make a conclusion regarding the stage shift of cancers by that time (Ministry of Health, Labour and Welfare 2023). Thus far, there have been three reports, including our own, concerning the impact of the COVID-19 pandemic on GI cancer diagnoses up to two years since the onset of the pandemic in Japan, with somewhat conflicting results obtained regarding stage shift (Iijima et al. 2023b; Miyamori et al. 2023; Kuzuu et al. 2023). Two prefecture-level population-based studies, including ours, using a hospital-based cancer registry did not find any notable change in the distribution of CRC stage in Hiroshima and Akita Prefectures (Iijima et al. 2023b; Miyamori et al. 2023) or in that of the EGC stage in Akita Prefecture (Iijima et al. 2023b). In contrast, a report using data collected from two high-volume hospitals in Yokohama City found a significant stage shift toward advanced stages of GCs and CRCs in 2021 (Kuzuu et al. 2023).

In the current study, we investigated the impact of the pandemic on GI cancer diagnoses for the first three years of the outbreak. The total number of EGCs diagnosed since the onset of the pandemic continued to be lower than the pre-pandemic level, which might suggest, at a glance, a failure to identify undiagnosed cancers due to the ongoing disruption of the healthcare system. However, considering the long-term trends in the annual number of diagnosed GI cancers in our area since 2011 (Fig. 4), when the current registration system started, the total number of both GCs and ECs, especially for GCs, was already on the decline even before the pandemic began. Meanwhile, as we recently reported, the number of diagnostic procedures, such as endoscopic examinations, quickly recovered in our area a few months after the pandemic began (Iijima 2023a). The apparent insufficient recovery of the total number of EGCs after the pandemic may thus be largely due to its long-term declining trend rather than a failure to overcome the problems associated with a delayed diagnosis. Supporting this view, there was no notable trend in a stage shift towards more advanced EGCs after the pandemic in comparison with the pre-pandemic baseline.

On the other hand, the total number of diagnosed CRCs in the first three years of the pandemic exceeded that in the previous three years. Considering that the annual number of CRCs had been relatively stable over the last decade in our area (Fig. 4), this finding suggests that the identification rate of undiagnosed CRCs that occurred in the first year of the pandemic had returned to the pre-pandemic baseline within the first three years of the pandemic. In addition, as with EGC, there is no trend in a stage shift toward more advanced CRC.

Thus, our current survey examining the three-year period of the pandemic shows that the disturbance of GI cancer diagnoses by the pandemic seems to have settled down without any substantial disease progression. In addition, there was no change in the proportion of initial cancer treatment before or during the pandemic in this study.

This is a survey from a single prefecture in Japan; we must therefore wait for a final report using a nationwide survey to estimate the ultimate impact of the COVID-19 pandemic on cancer treatment. However, our early report from Akita Prefecture will provide valuable information to the rest of the country, as the impact of the pandemic on GI cancer care should have been most evident in our area, considering that Akita Prefecture has had the highest GI cancer incidence and mortality in the nation for several years (Koizumi et al. 2018a, b), and because the diagnostic procedure for GI cancer was uniformly suspended throughout the country during the initial phase of the pandemic (Okuyama et al. 2022; Iijima et al. 2022, 2023b).

There are several potential reasons for the relative maintenance of GI cancer care with minimal disruption during the pandemic in Japan. First, the magnitude of the infection was much lower in Japan than in many other countries, especially during the initial phase of the pan-

demic. We were therefore able to take the necessary measures to prepare for the ongoing infection. Second, specifically for GI cancers, digestive endoscopy, a mandatory diagnostic procedure for cancers, was promptly resumed after only a few months of partial suspension during the initial phase of the pandemic, and it has never been suspended in Japan since then (Irisawa et al. 2020; Iijima et al. 2023a). Finally, the universal health insurance system in Japan likely had general, fundamental impacts on preventing disparity in access to healthcare systems during the pandemic, as has been observed in several other countries (Lofters et al. 2023; Negoita et al. 2024).

The total number of diagnosed HBP cancers did not show any signs of decrease, even during the pandemic, mainly because of the natural increasing trend in these types of cancers in our area, as in the whole nation. Despite this, the steady increase in the number of the most advanced HBP cancers (stage IV) after the pandemic is a somewhat unexpected phenomenon. Since there is no screening procedure for HBP cancers, patients' hesitation to visit hospitals due to fears of infection despite emerging symptoms may be responsible for this phenomenon (Inoue et al. 2023). Indeed, infection with a new omicron variant of COVID-19 was rampant in 2022 in Akita Prefecture, as well as throughout Japan. Although some studies reported an impact on diagnoses of HBP cancers up to two years after start of the pandemic in Japan (Kasuga et al. 2023; Murai et al. 2024), further population-based monitoring of the trend of HBP cancers is required.

In conclusion, this is the first population-based study to follow the real impact of the COVID-19 pandemic on GI cancer diagnoses up to three years into the outbreak. The disruption of GI cancer diagnoses caused by the pandemic is settling down without any substantial disease progression, even in Akita Prefecture, Japan, the area with the highest incidence of GI cancers in the country. In future infectious disease pandemics, ensuring the early resilience of healthcare systems and encouraging patients to undergo medical examinations will be important to avoid increasing mortality from GI cancers.

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