

Epidemiological Trends and Future Perspectives of Gastric Cancer in Eastern Asia

Masau Sekiguchi^{a, b, c, d} Ichiro Oda^{b, e} Takahisa Matsuda^{a, b, c} Yutaka Saito^b

^aCancer Screening Center, National Cancer Center Hospital, Tokyo, Japan; ^bEndoscopy Division, National Cancer Center Hospital, Tokyo, Japan; ^cDivision of Screening Technology, Center for Public Health Sciences, National Cancer Center, Tokyo, Japan; ^dDivision of Surgery, Department of Clinical Sciences, Danderyd Hospital, Karolinska Institutet, Stockholm, Sweden; ^eDepartment of Internal Medicine, Kawasaki Rinko General Hospital, Kawasaki, Japan

Keywords

Gastric cancer · Epidemiology · *Helicobacter pylori*

Abstract

Background: The global epidemiological situation of gastric cancer has changed considerably over time, and it is essential to understand the epidemiological trends and future perspectives of gastric cancer. **Summary:** Although gastric cancer was common in the United States less than a century previously, it is no longer common in this country. Currently, over 60% of gastric cancers are found in Eastern Asia. In some Eastern Asian countries such as Japan and Korea, population-based gastric cancer screening has been conducted using upper gastrointestinal endoscopy or radiography to lower gastric cancer mortality. Due to earlier detection of gastric cancer, the survival of patients with gastric cancer is more favorable in these countries than in other Western countries. Even in Eastern Asia, a remarkable decrease in the age-standardized incidence and mortality of gastric cancer has been observed. This downward trend is mainly due to the reduced *Helicobacter pylori* infection, and this trend is considered to continue. Nevertheless, both the absolute number of inci-

dent cases and deaths of gastric cancer are still increasing at present due to the aging population. For the time being, the management of gastric cancer in elderly population is a critical issue in Eastern Asia. The absolute numbers of gastric cancer cases and deaths are believed to peak in the near future, following the decreasing age-standardized incidence and mortality. **Key Messages:** After a long period, gastric cancer may become a rare cancer even in Eastern Asia, and new efficient approaches for its prevention, screening, and treatment are warranted.

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Introduction

The global burden of gastric cancer seems to be lower than that of other cancers, such as lung and colorectal cancers [1–5]. However, many gastric cancer cases are still newly detected, particularly in high-risk Eastern Asian countries [1–5]. In this situation, it is essential to understand the epidemiological trends and future perspectives of gastric cancer. In this study, these issues were reviewed.

Table 1. Top 5 cancers in terms of the global incidence and mortality in 1990 and 2020 based on the data from the Global Cancer Observatory: Cancer Today

	Year 1990	Year 2020
Incidence		
1	Lung cancer (<i>n</i> = 1,036,900)	Breast cancer (<i>n</i> = 2,261,419)
2	Stomach cancer (<i>n</i> = 798,300)	Lung cancer (<i>n</i> = 2,206,771)
3	Breast cancer (<i>n</i> = 795,600)	Colorectal cancer (<i>n</i> = 1,931,590)
4	Colorectal cancer (<i>n</i> = 782,800)	Prostate cancer (<i>n</i> = 1,414,259)
5	Liver cancer (<i>n</i> = 437,400)	Stomach cancer (<i>n</i> = 1,089,103)
Mortality		
1	Lung cancer (<i>n</i> = 921,000)	Lung cancer (<i>n</i> = 1,796,144)
2	Stomach cancer (<i>n</i> = 628,000)	Colorectal cancer (<i>n</i> = 935,173)
3	Colorectal cancer (<i>n</i> = 437,000)	Liver cancer (<i>n</i> = 830,180)
4	Liver cancer (<i>n</i> = 427,000)	Stomach cancer (<i>n</i> = 768,793)
5	Breast cancer (<i>n</i> = 314,000)	Breast cancer (<i>n</i> = 684,996)

Global Trend on the Incidence and Mortality of Gastric Cancer

The global epidemiological situation of gastric cancer has changed considerably over time [1–4]. Less than a century previously, gastric cancer was reportedly the most common cancer worldwide, even in the United States. However, it is well known that gastric cancer is no longer common in the United States and Western countries. Over 60% of the new gastric cancer cases are observed in Eastern Asia [5].

The global burden of other cancers, such as lung and colorectal cancers, is believed to be higher than that of gastric cancer [5]. According to the Global Cancer Observatory: Cancer Today statistics by the International Agency for Research on Cancer (IARC), gastric cancer showed the second highest incidence and mortality worldwide in 1990 [6, 7], whereas in 2020, gastric cancer was the fifth most common cancer with the fourth highest mortality rate [5] (Table 1). The age-standardized incidence and mortality of gastric cancer have decreased globally, reflecting the lower burden of gastric cancer [1–4]. The Global Burden of Disease Study (GBD) 2017 showed that the global age-standardized incidence decreased by 28.0% in 2017 compared with that in 1990, and the age-standardized mortality decreased by 48.7%, and this decreasing trend was most remarkable in high-income Asian countries such as Japan and South Korea [4].

Despite the remarkable downward trend in the age-standardized incidence and mortality of gastric cancer, both the absolute number of incident cases and deaths of

gastric cancer are still increasing due to population aging [4]. According to GBD 2017, the number of worldwide incident cases increased from approximately 864,000 in 1990 to 1.22 million in 2017, and the number of deaths increased from approximately 769,000 in 1990 to 865,000 in 2017 [4]. In this context, it is believed that management of gastric cancer, particularly in the elderly population, continues to be an important issue for a while, although the decreasing trend of age-standardized incidence and mortality is expected to be followed by a decrease in the absolute numbers of gastric cancer cases and deaths from long-term perspectives.

The survival rate for gastric cancer has improved worldwide over the years owing to improvements in diagnosis and treatment [3, 8]. However, it is still difficult to state that the survival rate is favorable worldwide. According to a report from the global surveillance of trends in cancer survival programs, the age-standardized 5-year net survival rate for gastric cancer still ranges between 20 and 40% in many countries [8]. For instance, the age-standardized 5-year net survival rates for patients with gastric cancer in 2010–2014 are reportedly 33.1% in the United States and 20.7% in the UK [8]. In these countries, gastric cancers tend to be detected at an advanced stage. In contrast, the age-standardized 5-year net survival rates are higher in South Korea and Japan. The survival rates for patients with gastric cancer in 2010–2014 are reportedly 68.9% in South Korea and 60.3% in Japan [8]. Early detection of gastric cancer is considered to have contributed to favorable survival in these countries.

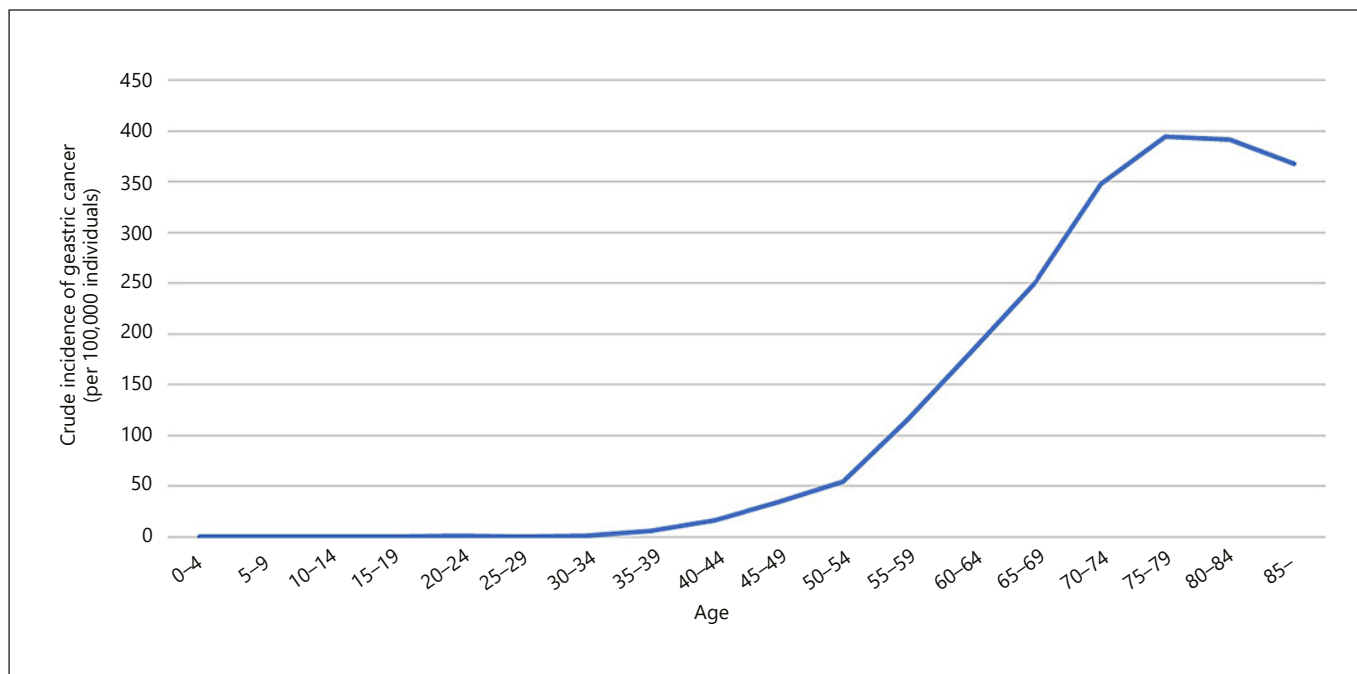


Fig. 1. Crude gastric cancer incidence by age in Japan in 2012 based on the data from 3 prefectures with high-quality data registries.

Trend on the Incidence and Mortality of Gastric Cancer in Japan

In Japan, the incidence and mortality of gastric cancer are high, and gastric cancer is an important target for screening and treatment. The most updated data from the cancer registry and statistics in Japan have shown that gastric cancer ranks second in cancer incidence with 129,476 cases in 2017 and third in cancer mortality with 42,931 deaths in 2019 [9, 10]. Figure 1 shows the crude gastric cancer incidence by age in Japan (the incidence based on the data from 3 prefectures with high-quality data registries, Yamagata Prefecture, Fukui Prefecture, and Nagasaki Prefecture, is shown); it is evident that gastric cancer is more frequently detected in the elderly population [11, 12]. Because of the increasing number of the elderly population, the crude incidence rate of gastric cancer continues to increase. However, the age-adjusted incidence rate shows a downward trend, as demonstrated in Figure 2a (the age-adjusted incidence rate of gastric cancer in the previously mentioned 3 prefectures with high-quality data registries in Japan is shown) [11, 12]. Presumably due to the improvement of early detection and treatment outcomes, a more remarkable downward trend is observed for the

age-adjusted mortality rate of gastric cancer in Japan, as shown in Figure 2b (the age-adjusted mortality rate of gastric cancer based on the data from the Vital Statistics of Japan is described) [9, 12].

Risk Factors for Gastric Cancer

The decreasing trend of the age-adjusted incidence and mortality of gastric cancer is due to that of noncardia gastric cancer [1–4]. With respect to risk factors for gastric cancer, various factors have been examined, and IARC has described the risk factors in IARC Monographs based on existing evidence, as shown in Table 2 [13]. Among the factors, *Helicobacter pylori* is a major risk factor for gastric cancer, particularly for noncardia cancer, and the reduction of *H. pylori* infection has contributed to the decrease of noncardia gastric cancer [1–4, 14]. In Japan, the proportion of positive *H. pylori* infection has been high in individuals born before 1950; however, the positive proportion has become lower in individuals born after 1950 due to the improvement of the hygiene situation. Moreover, currently, the proportion is reportedly lower than 10% in children [15, 16]. It is estimated that the proportion has decreased by 10–15% per 10 years in

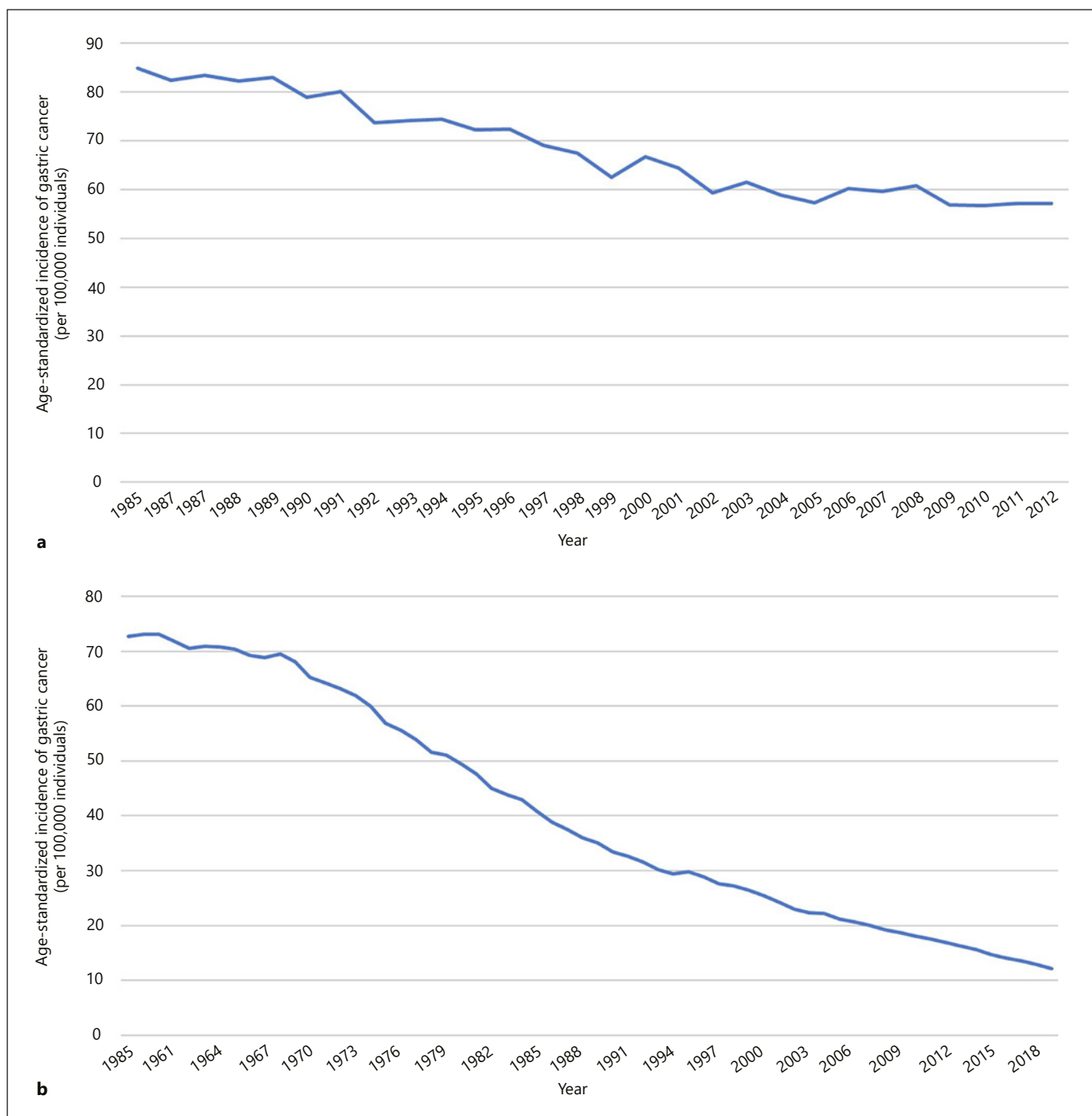


Fig. 2. a Time trend of age-standardized incidence rate of gastric cancer in Japan based on the data from 3 prefectures with high-quality data registries. **b** Time trend of age-standardized mortality rate of gastric cancer in Japan based on the data from the Vital Statistics of Japan.

every age-group and that this decreasing trend will lead to a further decrease in gastric cancer in Japan.

Although the incidence of noncardia cancer has decreased, cardia cancer has reportedly increased, especial-

ly in developed countries [17]. Cardia cancer has different risk factors from noncardia cancer, such as body fatness, and cardia cancer may become a more frequent subtype, even in Eastern Asia, in the future.

Table 2. Risk factors for gastric cancer described in the IARC Monographs

Agents with sufficient evidence in humans	Agents with limited evidence in humans	
<i>H. pylori</i>	Asbestos	Opium
Rubber production industry	Epstein-Barr virus	Pickled vegetables
Tobacco smoking	Lead compounds and inorganic	Processed meat
X-radiation and gamma-radiation	Nitrate or nitrite	Salted fish and Chinese style

Gastric Cancer Screening

The survival rate for gastric cancer is better when it is detected at earlier stages, and screening for gastric cancer is expected to lower gastric cancer mortality through early detection. Gastric cancer screening is conducted in high-risk countries, such as Japan and South Korea, to lower gastric cancer mortality.

In Japan, previously, only upper gastrointestinal X-ray screening was used, and endoscopy screening was not adopted because of the lack of evidence on its gastric cancer mortality reduction effect. However, after the following studies proved the mortality reduction effect of gastric cancer screening using endoscopy, endoscopy screening was accepted as a population-based screening method in Japan in 2016 [18–21]. A case-control study assessing the effectiveness of endoscopic screening for gastric cancer in a Japanese island (Kamigoto town, Kamigoto Island) has shown a significantly lower risk of gastric cancer death in individuals who underwent endoscopic screening within 5 years compared with those who did not undergo it (odds ratio: 0.206, 95% confidence interval: 0.044–0.965) [18]. A community-based, case-control study evaluating mortality reduction from gastric cancer by endoscopic screening in Japan (4 cities in Tottori Prefecture and Niigata City) has also demonstrated a significant reduction in gastric cancer mortality by endoscopic screening compared with no screening within 36 months before the date of diagnosis of gastric cancer (odds ratio: 0.695, 95% confidence interval: 0.489–0.986) [19]. Thereafter, a large-scale nested case-control study using data from the Korean National Cancer Screening Program for gastric cancer clearly has shown the effectiveness of endoscopy screening to reduce gastric cancer mortality by comparing individuals who received screening endoscopy with those who did not receive screening (odds ratio: 0.53, 95% confidence interval: 0.51–0.56), whereas the effectiveness of upper gastrointestinal X-ray was not demonstrated (odds ratio: 0.98, 95% confidence interval: 0.95–1.01) [20]. Current-

ly, in Japan, endoscopy is recommended as a population-based screening modality for individuals aged 50 years and older, and significant effort has been made to conduct high-quality endoscopy screening [21].

Korea also has a national cancer screening program (the Korean National Cancer Screening Program), and gastric cancer screening with upper endoscopy or gastrointestinal X-ray has been provided every 2 years for all Koreans aged 40 years and older since 2005. As mentioned above, the effectiveness of screening, particularly with endoscopy, was proven using large-scale data from the Korean National Cancer Screening Program [20].

With the current high prevalence of gastric cancer in these countries, gastric cancer screening for all populations of a certain age is expected to play an essential role in lowering gastric cancer mortality. However, as the prevalence of gastric cancer decreases in the future, it may become subsequently inefficient to continue the current style of population-based gastric cancer screening. The effectiveness of screening for all populations of a certain age may become less effective compared to its work burden. Population-based cancer screening should be safe and effective; in addition, favorable cost-effectiveness and reasonable work burden are essential [22, 23]. In this sense, the necessity and method of gastric cancer screening should always be discussed according to the prevalence of gastric cancer and the situation of risk factors such as *H. pylori* in the future [24]. The time is presumably approaching when a more risk-stratified screening approach with consideration of the status of risk factors, particularly the status of *H. pylori*, should be considered.

Management of Elderly Patients with Gastric Cancer

In Eastern Asia, gastric cancer in the elderly population is a critical issue for the time being. Due to the increasing chances of screening and endoscopy, more early stage gastric cancers may be detected in elderly individuals.

With respect to early stage gastric cancer, if a lesion meets the conditions of negligible risk of lymph node metastasis (corresponding to the absolute and expanded indications of endoscopic resection stated in the current treatment guidelines), endoscopic treatment such as endoscopic submucosal dissection is performed for the lesion [25, 26]. If a lesion does not meet the conditions and is considered to have even a slight risk of lymph node metastasis (>1%), surgical gastrectomy with lymphadenectomy is principally recommended for the lesion even in elderly patients [25, 26]. However, surgical gastrectomy may be significantly invasive in not a few elderly patients, considering their limited life expectancy, the risk of adverse events from surgery, and the influence of surgery on their quality of life [27–29]. To avoid overtreatment with gastrectomy, new indications for endoscopic resection are warranted in elderly patients, and clinical research to examine this issue is ongoing [30]. With respect to additional surgery following endoscopic resection, more individualized care considering the metastatic risk of gastric cancer based on the pathological results of endoscopically resected specimens is gradually preferred in the management of elderly patients [25, 26, 30, 31]. Further efforts to provide less invasive and more individualized care for elderly patients are required.

Future Perspectives

Due to the further reduction of *H. pylori* infection and improvement of environment-related factors, the downward trend in the age-standardized incidence and mortality of gastric cancer is believed to continue in Eastern Asian countries. Furthermore, this trend is considered to lead to a decrease in the absolute numbers of gastric cancer cases and deaths. In Japan, based on the estimation by Cancer Information Services, National Cancer Center, Japan, the absolute number of gastric cancer cases is predicted to peak during 2030–2034 for men and during 2025–2029 for women [12]. After the peak-out, the decreasing trend of gastric cancer may become more remarkable.

Even with the decreasing trend, it is difficult to completely extinguish gastric cancer even after a long period, as gastric cancer is still found currently in Western countries. Different subtypes of gastric cancer, such as *H. pylori*-negative cancer and cardia cancer, may be more frequently observed in the future. Prevention and management with more consideration of these different subtypes will be necessary.

Conclusion

Gastric cancer may be rare in Eastern Asia in the future. As a result, gastric cancer screening targeting all populations of a certain age may become inefficient; however, the importance of early detection and treatment of gastric cancer will never change, and new efficient strategies for the prevention, screening, and treatment of gastric cancer are warranted. For the time being, many patients still have gastric cancer and premalignant conditions, particularly elderly patients, in Eastern Asia, and efforts to provide appropriate medical care for these individuals are essential.

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Masau Sekiguchi, Ichiro Oda, Takahisa Matsuda, and Yutaka Saito designed the study. Masau Sekiguchi drafted the article. All the authors contributed to the interpretation of the data. Ichiro Oda, Takahisa Matsuda, and Yutaka Saito contributed to the critical revision of the article for important intellectual content. All the authors approved the final version of the article, and agree to be accountable for all aspects of the work.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed.

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