



Adequate period of surveillance in each stage for curatively resected gastric cancer: analyzing the time and rates of recurrence

Akikazu Yago¹ · Shusuke Haruta¹ · Masaki Ueno¹ · Yosuke Hamada¹ · Yusuke Ogawa¹ · Yu Ohkura¹ · Masayuki Urabe¹ · Harushi Udagawa¹

Received: 5 June 2020 / Accepted: 8 December 2020 / Published online: 5 January 2021
© The International Gastric Cancer Association and The Japanese Gastric Cancer Association 2021

Abstract

Background Surveillance after curative surgery for gastric cancer is conventionally performed for 5 years. However, the appropriate follow-up period remains controversial.

Methods This study retrospectively compiled a clinicopathological database of patients who underwent curative gastrectomy between 1975 and 2010 at Toranomon Hospital and were reviewed until March 2020. Analyzing the follow-up rate and recurrence rate for each stage in each postoperative year, we set each follow-up endpoint when the subsequent recurrence rate fell below 1%.

Results A total of 5235 patients were eligible for inclusion in the study. The rate of patients followed up for 5 years was 90.3%. The rates of follow-up were 52.7% at 10 years, 38.3% at 15 years, and 10.3% at 20 years. Recurrence was confirmed in 850 patients in total (16.2%) and in 50 patients beyond 5 years. The adequate follow-up endpoints according to stage (with < 1% recurrence risk) were 2 years for stage IA, 4 years for IB, 6 years for IIA, 9 years for IIB, 7 years for IIIA, and 8 years for IV (curative). For stage IIIB and IIIC, the recurrence risk remained.

Conclusions The adequate surveillance duration of resected gastric cancer might be different in each stage. Although the follow-up duration for stage I disease could be reduced to less than 5 years, advanced gastric cancer such as stage III or IV disease has risk of recurrence beyond 5 years and therefore additional follow-up is required. These results could help decide the strategy for surveillance.

Keywords Gastric cancer · Surveillance · Gastrectomy · Recurrence · Curative resection

Introduction

Surgeons are sometimes faced with the unresolved issue of deciding the follow-up strategy following curative surgery for gastric cancer [1]. Intervals and durations of surveillance differ based on the clinician's preference and institutional practice guidelines [2–5]. Recommendations in international guidelines include postoperative follow-up for most cancers, despite the fact that the role of follow-up in improving overall survival is not yet clear for all types of tumors. [6–9] Based on the Japanese gastric cancer treatment guidelines [10], most surgeons in Japan conventionally carry out

postoperative surveillance for gastric cancer after curative surgery for 5 years. However, it remains controversial as to whether surveillance as a specific follow-up strategy can provide survival advantage by means of early identification, how often recurrences occur in each postoperative year and how long patients should receive surveillance.

Surgeons sometimes encounter patients with recurrence beyond 5 years post-gastrectomy, even when the patients had been disease-free for 5 years. However, there are few reports of recurrence beyond 5 years post-gastrectomy because the follow-up programs usually end in 5 years and curability postoperatively is often estimated with the 5-year survival rate [11, 12]. Previous reports have indicated that recurrence after gastric resection occurs within the first 3 years in most cases [1, 13, 14]. Nevertheless, the efficacy of surveillance for gastric cancer had not been adequately proven. Several studies have shown that follow-up after gastric cancer resection provides no evident survival benefit [15], intensive

✉ Shusuke Haruta
shusuke-haruta@umin.ac.jp

¹ Department of Gastroenterological Surgery, Toranomon Hospital, 2-2-2 Toranomon, Minato-ku, Tokyo 105-8470, Japan

follow-up did not significantly influence overall survival [16], and a shorter surveillance interval was not beneficial for improved survival [17].

In contrast, intensive surveillance after curative resection of colorectal cancer has been demonstrated to improve overall survival [18–21]. According to the Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines for treatment of colorectal cancer [22] the recommended period of surveillance is 5 years, as for most patients recurrence is usually detected within 5 years post-gastrectomy and the incidence of recurrence beyond this is less than 1%. While the oncological features of gastric cancer differ from those of colorectal cancer, advances in various treatments for gastric cancer have made it pertinent to re-assess the significance of surveillance for resected gastric cancer.

Our department has data on many patients with long-term follow-up beyond 5 years, including screening test data, and we have maintained a robust database since 1975. In this study, we therefore analyzed the accumulated data on recurrence following curative resection for gastric cancer in each pathological stage to evaluate the adequate duration of surveillance for detecting recurrence in this patient population.

Methods

Population

We analyzed clinical and pathological information input into our database of patients who underwent gastrectomy between 1975 and 2010 at the Department of Gastroenterological Surgery, Toranomon Hospital. In principle, gastrectomy was performed with concurrent D1 + lymph node dissection (for early stage gastric cancer) or D2 lymph node dissection (for advanced disease). Patients fulfilled the criteria for histologically proven gastric cancer and macroscopically curative resection. Staging and histopathological grading were performed based on the 3rd edition of the Japanese Classification of Gastric Carcinoma [23]. Patients were categorized as stage IA, IB, IIA, IIB, IIIA, IIIB, IIIC, or IV with curative resection. The collected data included age, sex, surgical procedure, method of approach, location, invasion depth, lymph node metastasis, distant metastasis, and histologic type.

Methods of surveillance

Follow-up evaluation was based on history, findings on clinical examination, results of blood tests including tumor markers, and findings on imaging studies and endoscopy. Blood examination was repeated at 3-month interval in postoperative year 1 and every 3 or 6 months thereafter. Computed tomography (CT) was carried out every 6 months, with

yearly endoscopy as screening for cancer in the gastric remnant. In addition to this routine follow-up regimen, patients consulted us if they had clinical symptoms that raised suspicion of disease recurrence. For suspected metastasis to bone, brain, lung, and/or other sites, bone scintigraphy, chest or brain CT, or positron emission tomography-CT were performed. We regarded recurrence sites undetected by these modalities as not being recurrence, continued the surveillance examination, and diagnosed the recurrence when confirming obvious abnormal lesions.

The period under review in this study was from January 1975 to March 2020. Patients' records were documented until disease recurrence or until the last date they were confirmed to have been alive with no recurrence. The duration of follow-up was defined as the interval between surgery and the last documented review. For patients with gastric cancer recurrence, the duration of follow-up was defined as the interval between surgery and recurrence.

After recurrence was detected, appropriate treatments including chemotherapy were administered at the discretion of the treating surgeons, regardless of the pattern such as local recurrence, peritoneal dissemination, liver metastasis, or/and distant metastasis. Recurrence was defined only by a reappearance of primary gastric cancer. The second primary cancer in the stomach or non-gastric cancer were not classified as recurrence in this study, because our focus was on recurrence of the resected primary lesion.

Definition of the adequate follow-up duration

We named the recurrence rate that would occur beyond the specified time point as the “future recurrence rate”. This rate was calculated by subtracting the number of cases that already had recurrence from the total number of recurrences. In this study, the adequate follow-up period was defined as the length of time it took for the future recurrence rate to fall below 1%, designated the “follow-up endpoint”. Under the JSCCR guidelines [22], the premise of 5 years of surveillance is based on the less than 1% incidence of recurrence beyond 5 years. Thus, we set the cut-off value as the time taken to reach less than 1% of the future recurrence rate.

Evaluations and statistical analysis

The primary endpoint of this study was the duration until the recurrence risk for each year fell to below 1%. We showed recurrence-free survival (RFS) and disease-free survival (DFS) using Kaplan–Meier analysis in each pathological stage of gastric cancer. DFS is defined as the time to recurrence or death without recurrence. The recurrence risk was calculated in each postoperative year by stage. That denominator is the number of patients with remaining recurrence-free at the start of each interval, excluding the number of

censored cases, deaths without recurrence, and recurrent cases. The Clopper-Pearson method was used for the assessment of 95% confidence intervals (CIs).

Computations were performed using IBM SPSS Statistics ver. 23 (IBM Corp., Armonk, NY).

This study was conducted with approval from the Ethics Committee of Toranomon Hospital (approval no. 1396).

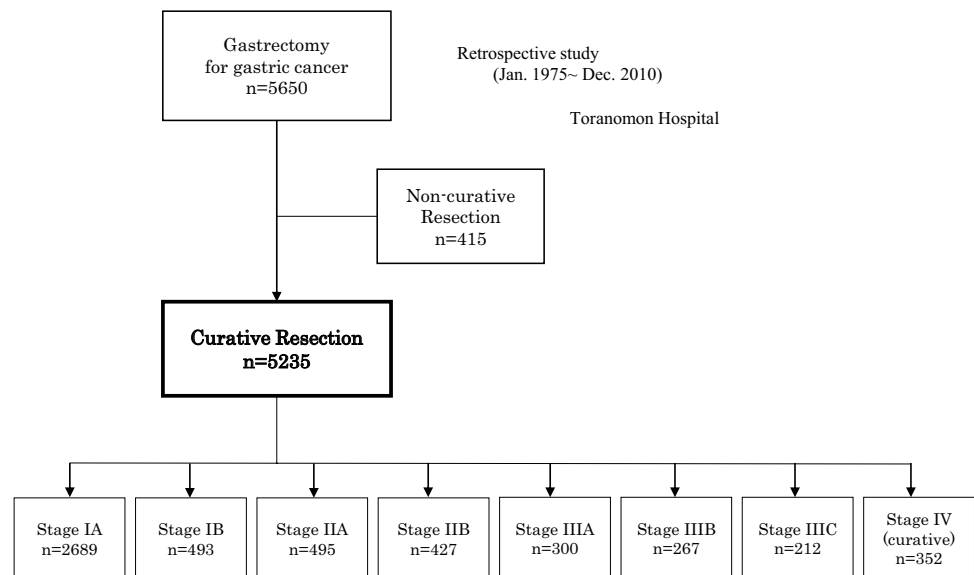
Results

Patient characteristics

Figure 1 shows the study flow diagram. In total, 5650 patients were diagnosed as having gastric cancer and underwent gastrectomy. Exclusions were cases with non-curative resection (415 patients), which left 5235 patients eligible for this study.

Table 1 shows the demographics and tumor characteristics of these 5235 patients who underwent curative gastrectomy. Median age was 62 (range, 18–98) years and 72.5% of the patients were male. Total gastrectomy was performed in 30.8% of patients and the laparoscopic approach was used in 5.0%. In terms of the pathology, undifferentiated type was observed in 29.8% of patients; 6.7% had curatively resected distant metastasis, which is stage IV disease without residual tumor. On categorizing the patients based on the 3rd edition of the Japanese Classification of Gastric Carcinoma [6], stage IA was observed in 2689 patients (51.4%), stage IB in 493 (9.4%), stage IIA in 495 (9.5%), stage IIB in 427 (8.2%), stage IIIA in 300 (5.7%), stage IIIB in 267 (5.1%), stage IIIC in 212 (4.1%), and stage IV with curative resection in 352 (6.7%).

Fig. 1 A total of 5235 patients underwent curative gastrectomy for gastric cancer from 1975 to 2010. The number at each stage is shown



Recurrence-free survival and disease-free survival

RFS and DFS curves according to each stage are shown in Fig. 2. The 5-year RFS rate was 99.0% for stage IA, 97.0% for stage IB, 88.3% for stage IIA, 73.8% for stage IIB, 67.4% for stage IIIA, 55.7% for stage IIIB, 29.9% for stage IIIC, and 25.4% for stage IV (curative). Almost all patients died after recurrence, with a median survival time of 8 months. One patient who had mediastinal lymph node metastasis survived for 84 months after recurrence.

Follow-up rate

Follow-up rates are shown in Fig. 3. Overall, 90.3% of all patients with resected gastric cancer received surveillance for 5 years. A total of 506 patients were lost to follow-up (either stopped attending follow-up visits without notice or went to other hospitals for further follow-up) by the end of postoperative year 5, along with 218 patients of death without recurrence. The follow-up rate was 52.7% at 10 years, 38.3% at 15 years, 10.3% at 20 years, and 2.9% at 25 years.

Recurrence risk

The recurrence rates for each stage in each postoperative year are shown in Table 2. In total, 850 (16.2%) of the 5235 patients who had undergone curative resection developed recurrence. This table shows that cases of early gastric cancer, such as stage IA or IB, had low recurrence rates throughout the entire period. Conversely, advanced gastric cancer, especially stage III or IV, had relatively high recurrence rates in the early period. It is relatively rare that patients develop recurrence beyond 5 years post-gastrectomy; 50 of all the curatively resected cases developed recurrence after

Table 1 Clinicopathological features of patients who underwent curative gastrectomy

Variable		n	(%)
Median age, years (range)	62 (18–98)		
Sex	Male	3745	(71.54)
	Female	1490	(28.46)
Procedure	Total gastrectomy	1611	(30.77)
	Distal gastrectomy	3078	(58.80)
	Proximal gastrectomy	394	(7.53)
	Pylorus-preserving gastrectomy	172	(3.29)
Approach	Open	4991	(95.34)
	Laparoscopic	264	(5.04)
Location	Proximal	1225	(23.40)
	Distal	3787	(72.34)
	Diffuse	223	(4.26)
Histologic type	Differentiated	3674	(70.18)
	Undifferentiated	1561	(29.82)
Depth of invasion	T1a	1567	(29.93)
	T1b	1428	(27.28)
	T2	569	(10.87)
	T3	762	(14.56)
	T4a	828	(15.82)
	T4b	81	(1.55)
Lymph node metastasis	N0	2372	(45.31)
	N1	618	(11.81)
	N2	536	(10.24)
	N3	601	(11.48)
Distant metastasis	M0	4883	(93.28)
	M1	352	(6.72)
Stage	IA	2689	(51.37)
	IB	493	(9.42)
	IIA	495	(9.46)
	IIB	427	(8.16)
	IIIA	300	(5.73)
	IIIB	267	(5.10)
	IIIC	212	(4.05)
	IV	352	(6.72)

this point, most of which were advanced gastric cancers of stage IIB or higher disease. The period keeping over 1% of recurrence risk in all cases was 6 years post-gastrectomy. Figure 4 presents the shift of recurrence rates with 95% CIs in each 1-year interval for each stage. For stage I or II, the recurrence rate by year never exceeds 1% after 7 years. For stage III or IV, the rate could not reach keeping less than 1% even over 7 years.

Future recurrence rate

We calculated future recurrence rates based on the recurrence rate in each postoperative year. Future recurrence rates and the follow-up endpoint in each postoperative year are shown in Table 3, which indicates the time when over 99% of the patients would no longer develop recurrence. Also, Fig. 5 shows the shift of future recurrence rates with 95% CIs for each stage for 10 years. Each follow-up endpoint was observed at 2 years after primary surgery for stage IA, 4 years after for stage IB, 6 years after for stage IIA, 9 years after for stage IIB, 7 years after for stage IIIA, and 8 years after for stage IV without residual tumor. For stage IIIB and IIIC, the future recurrence rate could not achieve below 1% even for over 10 years.

Recurrence pattern

The pattern and rate of recurrence according to each postoperative period are shown in Table 4. Peritoneal dissemination was found to have the highest recurrence pattern rate within 5 years. Although the trends in recurrence rates for each site were similar in each postoperative period, the proportion of cases of hematogenous metastasis and lymph node metastasis beyond 5 years tended to increase, but the proportion of peritoneal dissemination beyond 5 years did not.

Discussion

Gastric cancer continues to be one of the main causes of cancer death in the world. Surgical treatment either as primary therapy for early stage disease or secondary treatment after chemotherapy for local advanced disease is a critical prognostic factor for this cancer. Recurrence is a common problem after gastrectomy and eventually leads to death. The main goal in proper follow-up for patients following curative surgery should be primarily to identify asymptomatic recurrence, such as local recurrence, liver or lung metastasis, lymph node metastasis, and peritoneal dissemination, at a treatable stage. This may lead to quick and effective treatment and improved long-term survival. Several international organizations and authors have reported reviews on surveillance post-gastrectomy [11, 15, 24], but previous reports state that surveillance did not provide survival benefit and did not adequately show the accurate frequency or timing of recurrence or the adequate follow-up duration.

It is currently unclear whether the follow-up period should be the same for early gastric cancer and advanced disease. If the timing and rate of recurrence differ at each stage, then the adequate follow-up time should also differ. Bilici et al. [14] demonstrated the patterns and time of recurrence after proximal gastrectomy at each stage I, II, and

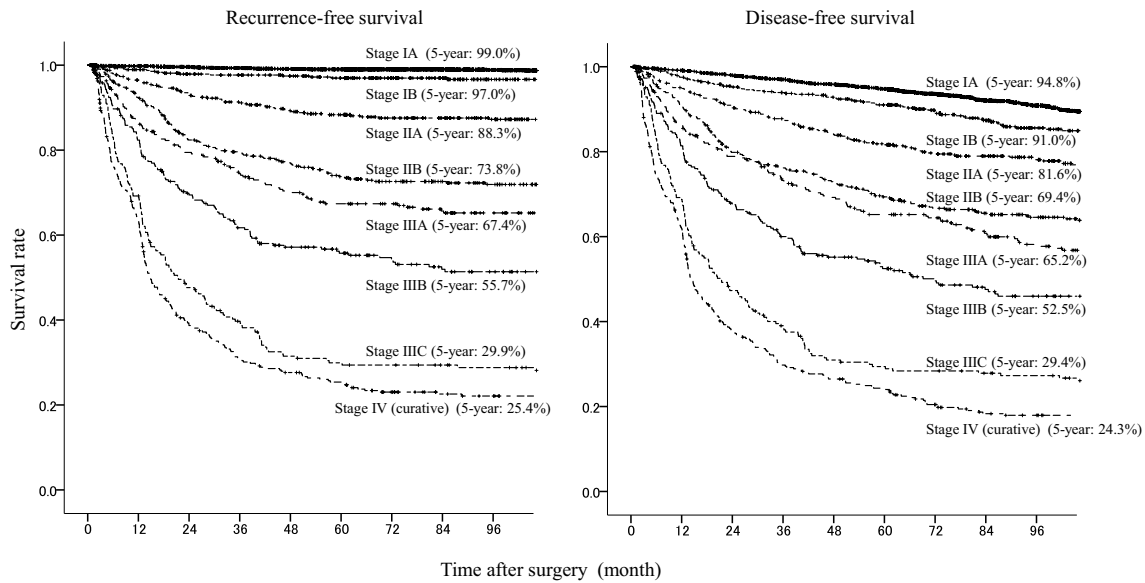


Fig. 2 Recurrence-free survival and disease-free survival curves with Kaplan–Meier analysis at each stage

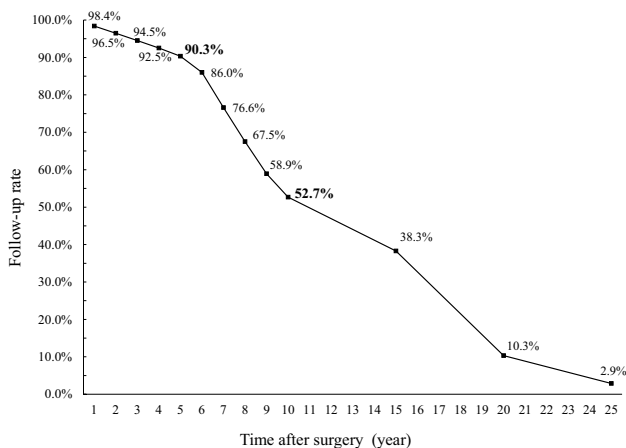


Fig. 3 Patients who received surveillance for 5 years amounted to 90.3%. The rate of follow-up was 52.7% at 10 years, 38.3% at 15 years, 10.3% at 20 years, and 2.9% at 25 years

III. Shiraishi et al. [25] reported on recurrence rates within 2 years and those beyond 2 years in stage I/II and stage III/IV, respectively. How the recurrence rates and time differ in each stage is poorly documented, however. In this study, we retrospectively reviewed the time and rates of recurrence after curative resection and systematic lymphadenectomy for gastric cancer, and we could successfully determine the adequate follow-up endpoint for each pathological stage.

As for all stages, the conventional follow-up period for 5 years seems reasonable because almost 99% of recurrences could be eliminated. As in previous reports [25–27], most recurrences of resected gastric cancer in our study tended to occur in the early stage, where more than 80% of recurrences

were detected within 3 years after the primary surgery. At the same time, our study additionally revealed that the adequate follow-up periods varied depending on stage; within 5 years for stage I and beyond 5 years for stage II, III, and IV disease. Most cases with early gastric cancer have an eliminated risk of recurrence at an early stage within 5 years, suggesting that it may be possible to shorten the period of surveillance. The European Society for Medical Oncology (ESMO) clinical guideline also indicated that follow-up should be tailored to the individual patient and the stage of the disease [28]. However, it is also necessary to keep in mind that even if patients are recurrence-free for 5 years post-gastrectomy, there is a chance of recurrence beyond 5 years. Also, attention should be paid to the fact that a slight possibility of subsequent recurrence remains for stage I disease due to the large population. Moon et al. [29] reported that 10.8% of 5-year survivors of advanced gastric cancer who underwent radical resection and adjuvant chemotherapy developed recurrence. Our study also showed that the late recurrence rate beyond 5 years would be relatively high in stage III disease, at 4.5% of those with 5-year recurrence-free survival. These risks of late recurrence suggest that it is better to prolong the period of surveillance in such cases. The rate of hematogenous and lymphogenous metastasis tended to increase but not that of peritoneal dissemination. The results of our study can help provide additional information to patients, and 99% of the recurrence risk can be eliminated in each stage when surveillance is terminated.

Our clinical practice of surveillance is based on the Japanese treatment guidelines for gastric cancer. Appropriate surveillance will provide an opportunity to treat recurrence before performance status worsens in the asymptomatic

Table 2 Recurrence risk for each stage in each postoperative year among patients with recurrence free at the start of each interval

Stage (n)	Recurrence risk in each postoperative year (n)										Over 10 years	
	1-year	2-year	3-year	4-year	5-year	6-year	7-year	8-year	9-year	10-year		
IA (2689)	1.19% (32)	0.19% (5)	0.19% (5)	0.28% (7)	0.21% (5)	0.13% (3)	—	0.12% (2)	0.14% (2)	0.08% (1)	0.19% (2)	
IB (493)	3.25% (16)	1.06% (5)	0.22% (1)	0.23% (1)	0.48% (2)	—	—	0.32% (1)	—	0.41% (1)	—	
IIA (495)	11.7% (58)	3.43% (17)	2.31% (10)	1.96% (8)	1.04% (4)	0.83% (3)	—	0.33% (1)	—	—	—	
IIB (427)	26.7% (114)	7.49% (32)	3.65% (12)	2.91% (9)	4.44% (12)	1.48% (4)	0.42% (1)	0.46% (1)	0.51% (1)	—	0.66% (1)	
IIIA (300)	32.7% (98)	13.0% (39)	6.19% (14)	5.39% (11)	4.21% (8)	—	2.41% (4)	0.68% (1)	—	—	—	
IIIB (267)	46.1% (123)	17.2% (46)	11.1% (19)	7.38% (11)	2.34% (3)	2.54% (3)	4.00% (4)	1.12% (1)	2.47% (2)	—	1.75% (1)	
IIIC (212)	70.3% (149)	30.7% (65)	16.3% (16)	20.5% (16)	4.92% (3)	1.75% (1)	—	1.96% (1)	2.08% (1)	—	3.03% (1)	
IV (352)	73.9% (260)	35.5% (125)	20.5% (26)	10.0% (10)	7.95% (7)	8.86% (7)	1.64% (1)	2.00% (1)	—	—	—	
All (5235)	16.2% (850)	6.38% (334)	2.41% (105)	1.72% (71)	1.08% (42)	0.49% (18)	0.32% (10)	0.32% (9)	—	0.09% (2)	0.27% (5)	

stage. Blood tests are performed to check tumor markers, nutritional changes, or/and other evidence of dysfunction. These tests are readily available, but their sensitivity and specificity to recurrence are not high. Annual endoscopy is effective in screening for recurrence at the anastomosis site or for detecting new lesions in the remnant stomach. Abdominal CT is used to detect intraabdominal recurrence. CT was reported to be the most useful investigation for detecting recurrence [17] and, indeed, many recurrences in our study were detected by CT, supported by additional investigations. The benefit of intensive surveillance after curative gastrectomy is reported to be limited, in contrast to that for colorectal cancer, because most curative treatment modalities may not be applicable for recurrent gastric cancer [17]. Unfortunately, almost all cases with recurrence in our series were ultimately mortalities. Although recently the prognosis after recurrence has improved gradually with advances in treatment regimens and the efficacy of chemotherapy for recurrent disease, it is still inadequate. Our study could not definitively indicate the effect of surveillance or early identification of recurrence on overall survival. However, various treatment methods including chemotherapy, radiotherapy, and immuno-oncology therapy have recently been developed. Hence, if the curability rates for some recurrent lesions improve, early detection of recurrence may lead to better prognosis for recurrent gastric cancer in the future.

In this study, we designated the adequate follow-up endpoint as the future recurrence rate falling below 1%. Currently, there is a paucity of evidence for determining this endpoint, so the accuracy of our designation could be controversial. However, we believe that it has some merit given the lack of major disagreement between our result and the conventional recommendation stated in the gastric cancer guidelines. Also, using this endpoint in our large dataset now makes it possible to tell patients some clearer information about how much recurrence risk remains, and doctors can utilize this information in surveillance. The validity of this cutoff point should also be considered from the viewpoint of cost-effectiveness. Although patients in our department tend to undergo long-term surveillance, it should be noted that continuing surveillance beyond 5 years to detect additional recurrence might cause psychosocial harm or impose economic burden on them. Kodera et al. [26] reported that early detection of asymptomatic gastric cancer recurrence did not improve overall survival and that close follow-up might not be cost-effective. These potentially unwanted influences from recurrence-focused surveillance should be taken into account.

A strength of our study is the uniform surgical approach that has remained essentially unchanged over the years due to practice in a single institution. Also, patients were managed with a consistent follow-up program over the long postoperative period, which allowed relatively accurate

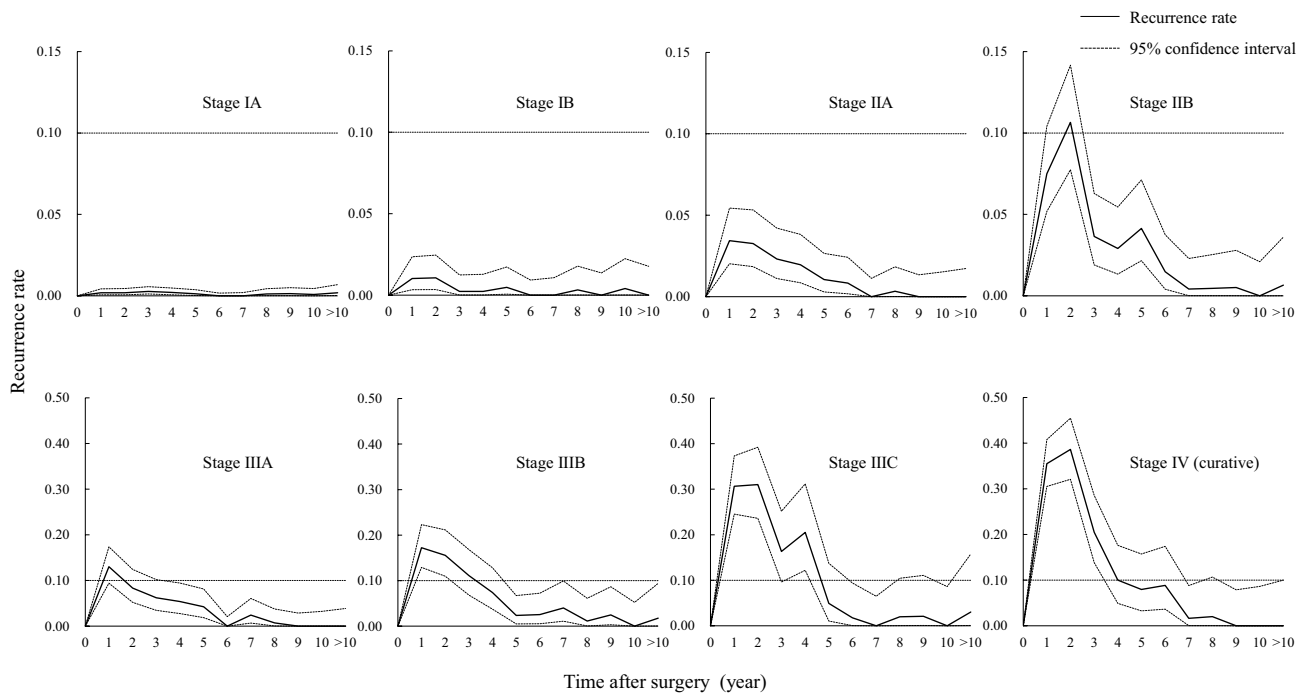


Fig. 4 Recurrence risk with 95% confidence intervals for each stage in each 1-year interval among patients with recurrence free at the start of each interval

identification of the clinicopathological features of the patients and the time, location, and frequency of recurrent disease.

This study also has various important limitations due to the large cohort studied, especially including many old cases. First, there is a possibility of occult recurrence in patients who are lost to follow-up, our calculation may have some bias and so may not provide an accurate assessment. However, among patients with recurrence after the end of follow-up, most returned to our department and received treatment. For this reason, we believe that our results would not provide a critical contradiction. Second, this was a retrospective study conducted at a single institution, so the number of cases with recurrence beyond 5 years is small. Therefore, obtained information has uncertainty in this study, and there might be different results if the sample size were increased. Third, the differences in clinical parameters of the patients could be confounders in this study. For example, transitions in the surgical methods or/and perioperative chemotherapy regimens might affect recurrence time. A meta-analysis showed that postoperative adjuvant chemotherapy may provide a benefit on overall survival and disease-free survival in gastric cancer compared with surgery alone [30]. Specifically, we started the addition of adjuvant chemotherapy with S-1 for patients with stage II and higher from 2000, because adjuvant chemotherapy had become the standard treatment [31]. We are assuming that the late recurrence rate would

not change significantly between before and after 2000, but further studies might be needed to confirm this. Ultimately, we focused on recurrence of resected primary gastric cancer in this study, so we did not include second primary cancers. Of course, regular endoscopy is required to detect new lesions and this would, by implication, be similar to a medical examination. While we eliminated regular endoscopy from surveillance for primary lesion recurrence, it is important to explain to the patient the risk of second primary cancer and recommend that they continue to receive regular medical examinations. We anticipate that future studies will help provide better follow-up strategies to improve overall and recurrence-free survival and to identify more effective markers and their ability to predict recurrence.

In conclusion, this study presented the recurrence rate in each postoperative year and the adequate follow-up endpoint. Although recurrence rate after postoperative year 5 was about 1% of all resected cases, the adequate surveillance duration of resected gastric cancer might be different in each stage. Thus, the follow-up period in stage I disease could be shortened if the adequate endpoint of surveillance is set considering less than 1% risk of recurrence. However, the risk of recurrence persists beyond 5 years in advanced gastric cancer such as stage III or IV disease, so additional surveillance might be required. These results could help decide the surveillance duration following curative resection of gastric cancer.

Table 3 Future recurrence risk among patients with recurrence free at the specified time point and follow-up endpoints

Stage (n)	Recurrence rate (n)	Future recurrence risk in each postoperative year (n)										Follow-up endpoint				
		1-year	2-year	3-year	4-year	5-year	6-year	7-year	8-year	9-year	10-year					
IA (2689)	1.19% (32)	1.03% (27)	0.87% (22)	–	–	–	–	–	–	–	–	–	–	–	–	2-year
IB (493)	3.25% (16)	2.34% (11)	1.35% (6)	0.96% (4)	–	–	–	–	–	–	–	–	–	–	–	4-year
IIA (495)	11.7% (58)	8.91% (41)	6.00% (26)	3.91% (16)	2.09% (8)	0.31% (1)	–	–	–	–	–	–	–	–	–	6-year
IIB (427)	26.7% (114)	21.3% (82)	12.5% (41)	9.39% (29)	6.90% (20)	2.96% (8)	1.83% (4)	0.57% (1)	–	–	–	–	–	–	–	9-year
IIIA (300)	32.7% (98)	23.3% (59)	16.8% (38)	11.8% (24)	6.84% (13)	3.01% (5)	0.68% (1)	–	–	–	–	–	–	–	–	7-year
IIIB (267)	46.1% (123)	36.3% (77)	25.7% (44)	16.8% (25)	10.9% (14)	8.00% (8)	4.49% (4)	3.70% (3)	1.45% (1)	–	–	–	–	–	–	None
IIIC (212)	70.3% (149)	57.9% (84)	39.8% (39)	29.5% (23)	11.5% (7)	5.45% (3)	5.88% (3)	4.17% (2)	2.44% (1)	–	–	–	–	–	–	None
IV (352)	73.9% (260)	62.8% (135)	40.9% (52)	26.0% (26)	18.2% (16)	3.28% (2)	2.00% (1)	0% (0)	–	–	–	–	–	–	–	8-year
All (5235)	16.2% (850)	10.9% (516)	6.15% (268)	3.96% (163)	2.36% (92)	1.35% (50)	0.82% (23)	–	–	–	–	–	–	–	–	7-year

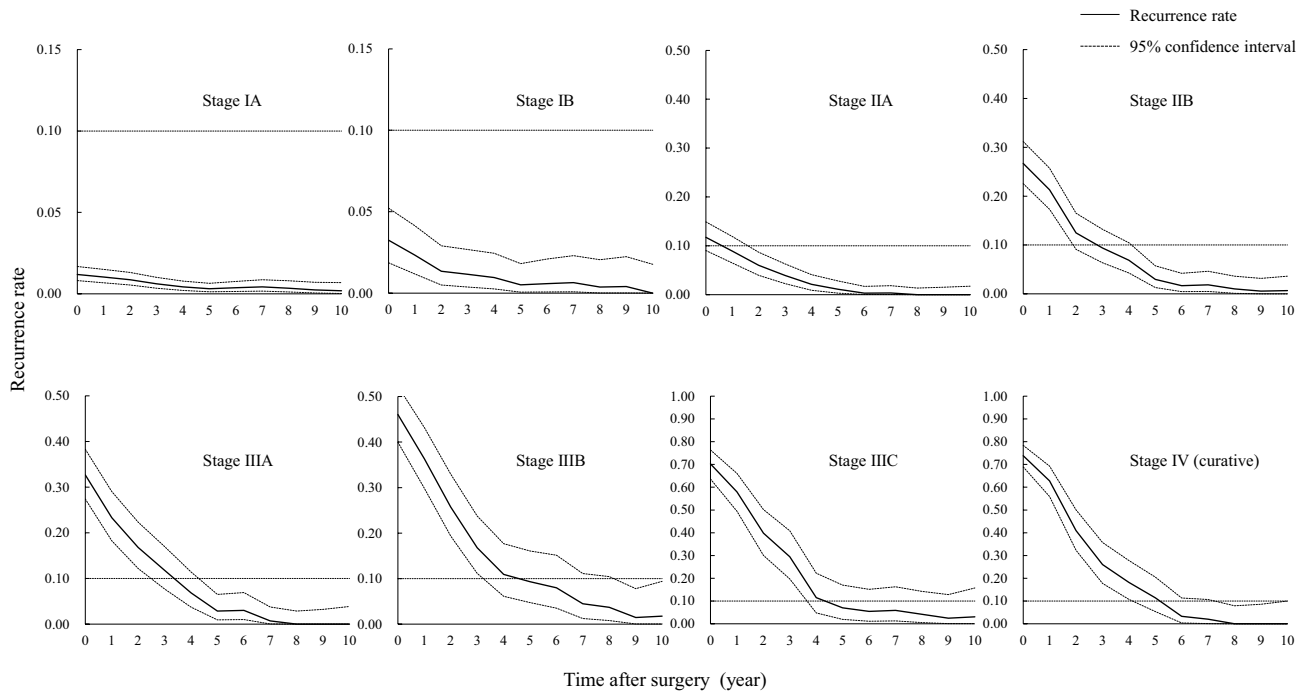


Fig. 5 Future recurrence risk with 95% confidence intervals for each stage among patients with recurrence free at the specified time point

Table 4 Pattern and rate of recurrence according to each postoperative period

Recurrence site	All recurrence cases ($n = 850$)		
	Within 3 years $n = 687$	4–5 years $n = 113$	Over 5 years $n = 50$
Lymph node metastasis	14.8%	12.4%	20.0%
Peritoneal dissemination	49.9%	55.8%	38.0%
Local recurrence	1.3%	2.7%	2.0%
Hematogenous metastasis	33.9%	29.2%	40.0%

Acknowledgments We thank Dr. Hiroyuki Ohbe, Department of Clinical Epidemiology and Health Economics, The University of Tokyo, for his helpful advice on statistical analyses.

Funding This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions.

References

1. D'Ugo D, Biondi A, Tufo A, Persiani R. Follow-up: the evidence. *Dig Surg.* 2013;30:159–68.
2. Kim H, Han S, Kim M, Hyung WJ, Kim W, Lee HJ, et al. Long-term results of laparoscopic gastrectomy for gastric cancer: a large-scale case-control and case-matched Korean multicenter study. *J Clin Oncol.* 2014;32:627–33.
3. Shinohara T, Satoh S, Kanaya S, Ishida Y, Taniguchi K, Isogaki J, et al. Laparoscopic versus open D2 gastrectomy for advanced gastric cancer: a retrospective cohort study. *Surg Endosc.* 2013;27:286–94.
4. Fang C, Hua J, Li J, Zhen J, Wang F, Zhao Q, et al. Comparison of long-term results between laparoscopy-assisted gastrectomy and open gastrectomy with D2 lymphadenectomy for advanced gastric cancer. *Am J Surg.* 2014;208:391–6.
5. Sato H, Shimada M, Kurita N, Iwata T, Nishioka M, Morimoto S, et al. Comparison of long-term prognosis of laparoscopy-assisted gastrectomy and conventional open gastrectomy with special reference to D2 lymph node dissection. *Surg Endosc.* 2012;26:2240–6.
6. National Comprehensive Cancer Network. Gastric cancer NCCN Guidelines. Available from: URL: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf.
7. Smyth EC, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D. Gastric cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2016;27:v38–49.
8. De Manzoni G, Marrelli D, Baiocchi GL, Morgagni P, Saragoni L, Degiuli M, et al. The Italian research group for gastric cancer (GIRCG) guidelines for gastric cancer staging and treatment 2015. *Gastric Cancer.* 2017;20:20–30.
9. Institut National du Cancer. Tumeur maligne, affection maligne du tissu lymphatique ou hématopoïétique. Available from: http://www.has-sante.fr/portail/upload/docs/application/pdf/2011-10/ald_30_gm_k_estomac_web.pdf.

10. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). *Gastric Cancer*. 2017;20:1–19.
11. Lee JH, Kim HI, Kim MG, Ha TK, Jung MS, Kwon SJ. Recurrence of gastric cancer in patients who are disease-free for more than 5 years after primary resection. *Surgery*. 2016;159:1090–8.
12. Maehara Y, Okuyama T, Oshiro T, Baba H, Adachi Y, Sugimachi K. Analysis of 390 patients surviving 10 years or longer after curative resection for gastric cancer. *Oncology*. 1994;51:366–71.
13. Kang WM, Meng QB, Yu JC, Ma ZQ, Li ZT. Factors associated with early recurrence after curative surgery for gastric cancer. *World J Gastroenterol*. 2015;21:5934–40.
14. Bilici A, Selcukbiricik F. Prognostic significance of the recurrence pattern and risk factors for recurrence in patients with proximal gastric cancer who underwent curative gastrectomy. *Tumour Biol*. 2015;36:6191–9.
15. Cardoso R, Coburn NG, Seevaratnam R, Mahar A, Helyer L, Law C, et al. A systematic review of patient surveillance after curative gastrectomy for gastric cancer: a brief review. *Gastric Cancer*. 2012;15(Suppl 1):S164–7.
16. Tan IT, So BY. Value of intensive follow-up of patients after curative surgery for gastric carcinoma. *J Surg Oncol*. 2007;96:503–6.
17. Park CH, Park JC, Chung H, Shin SK, Lee SK, Cheong JH, et al. Impact of the surveillance interval on the survival of patients who undergo curative surgery for gastric cancer. *Ann Surg Oncol*. 2016;23:539–45.
18. Renehan AG, Egger M, Saunders MP, O'Dwyer ST. Impact on survival of intensive follow up after curative resection for colorectal cancer: systematic review and meta-analysis of randomised trials. *BMJ*. 2002;324:813.
19. Figueredo A, Rumble RB, Maroun J, Earle CC, Cummings B, McLeod R, et al. Follow-up of patients with curatively resected colorectal cancer: a practice guideline. *BMC Cancer*. 2003;3:26.
20. Jeffery M, Hickey BE, Hider PN. Follow-up strategies for patients treated for nonmetastatic colorectal cancer. *Cochrane Database Syst Rev*. 2007;9:CD002200.
21. Tjandra J, Chan MK. Follow-up after curative resection of colorectal cancer: a meta-analysis. *Dis Colon Rectum*. 2007;50:1783–99.
22. Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines. for treatment of colorectal cancer. *Int J Clin Oncol*. 2014;25(20):207–39.
23. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. *Gastric Cancer*. 2011;14:101–12.
24. Whiting J, Sano T, Saka M, Fukagawa T, Katai H, Sasako M. Follow-up of gastric cancer: a review. *Gastric Cancer*. 2006;9:74–81.
25. Shiraishi N, Inomata M, Osawa N, Yasuda K, Adachi Y, Kitano S. Early and late recurrence after gastrectomy for gastric carcinoma univariate and multivariate analyses. *Cancer*. 2000;89:255–61.
26. Kodera Y, Ito S, Yamamura Y, Mochizuki Y, Fujiwara M, Hibi K, et al. Follow-up surveillance for recurrence after curative gastric cancer surgery lacks survival benefit. *Ann Surg Oncol*. 2003;10:898–902.
27. Lai JF, Kim S, Kim K, Li C, Oh SJ, Hyung WJ, et al. Prediction of recurrence of early gastric cancer after curative resection. *Ann Surg Oncol*. 2009;16:1896–902.
28. Smyth EC, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D, et al; ESMO Guidelines Committee. ESMO Guidelines Committee (2016) Gastric cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2016;27:38–49.
29. Moon YW, Jeung HC, Rha SY, Yoo NC, Roh JK, Noh SH, et al. Changing patterns of prognosticators during 15-year follow-up of advanced gastric cancer after radical gastrectomy and adjuvant chemotherapy: a 15-year follow-up study at a single Korean institute. *Ann Surg Oncol*. 2007;14:2730–7.
30. Paoletti X, Oba K, Burzykowski T, Michiels S, Ohashi Y, Pignon JP, et al; The GASTRIC Group. Benefit of adjuvant chemotherapy for resectable gastric cancer: a meta-analysis. *JAMA*. 2010;303:1729–37.
31. Sakuramoto S, Sasako M, Yamaguchi T, Kinoshita T, Fujii M, Nashimoto A, et al; ACTS-GC Group. Adjuvant chemotherapy for gastric cancer with S, an oral fluoropyrimidine. *N Engl J Med*. 2007;357:1810–20.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.