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Exploratory study on the impact of intraesophageal pressure on quality of life in patients following total gastrectomy: a retrospective cohort study

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Abstract

Background The usefulness of high-resolution impedance manometry (HRIM) in patients who underwent total gastrectomy with Roux-en-Y (R-Y) anastomosis has never been well validated. This study aimed to investigate whether intraesophageal pressure affects quality of life in patients who underwent total gastrectomy with R-Y anastomosis.

Methods The participants comprised 12 patients who underwent total gastrectomy for gastric cancer between October 2014 and July 2022 and underwent a postsurgical HRIM examination. The association between the HRIM data and Postgastrectomy Syndrome Assessment Scale-37 (PGSAS-37) questionnaires was analyzed.

Results Esophageal body motility was normal in almost all patients. The anastomosis shape (circular stapler and overlap method with linear stapler) did not influence intraesophageal pressure. The integrated relaxation pressure and lower esophageal sphincter (LES) residual pressure during swallowing-induced relaxation were involved in "diarrhea subscale" scores (p = 0.0244 and p = 0.0244, respectively). The average maximum intrabolus pressure was not involved in postgastrectomy symptom. The contractile front velocity correlated with the "indigestion subscale," "diarrhea subscale," and "constipation subscale" (p = 0.0408, p = 0.0143, and p = 0.0060, respectively). The distal latency, i.e., the time from upper esophageal sphincter relaxation to contractile deceleration, was also associated with the "abdominal pain subscale" (p = 0.0399). LES pressure and esophageal body motility affected patients' quality of life after total gastrectomy.

Conclusions HRIM for the evaluation of intraesophageal pressure is useful for the functional assessment of esophagojejunostomy with the R-Y reconstruction after total gastrectomy.

Keywords Intraesophageal pressure, Total gastrectomy, Gastric cancer, Postgastrectomy syndrome assessment scale-37, High-resolution impedance manometry, Lower esophageal sphincter

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Introduction

The exacerbation of quality of life (QOL) in patients due to postoperative gastric disorders, including abdominal distension, nausea, frequent vomiting, drowsiness, restricted food intake, weight loss, diarrhea, and decreased physical activity, is a serious clinical complication of gastrectomy for gastric cancer patients [1, 2]. Furthermore, the deterioration in daily life due to gastrectomy varies based on the type of surgical procedure. Therefore, proximal gastrectomy is increasingly recommended for Siewert type II gastroesophageal junction cancers that are < 4 cm in length [3]; however, total gastrectomy is mandatory for the curative resection of widely advanced or multiple gastric cancers despite its adverse effects on health and QOL [4]. Total gastrectomy results in the most pronounced postoperative disability among gastrectomy procedures; therefore, reducing the occurrence of this syndrome should be discussed when selecting the reconstruction method. Among the several reconstruction methods used following total gastrectomy, the Roux-en-Y (R-Y) reconstruction is a simple and still the most preferred technique. The R-Y reconstruction was first reported in 1947 and has been commonly used [5]. However, this approach often fails to prevent various symptoms after gastrectomy, negatively affecting the patient's QOL and ultimately leading to malnutrition.

Consequently, many reconstruction methods after total gastrectomy have been used; however, no optimal reconstruction method has been universally accepted, causing an age-long debate [6]. Although creating a pouch with reservoir capacity instead of the stomach may reduce the incidence of early and late dumping symptoms, its usefulness has not been fully demonstrated in several clinical trials, including randomized controlled trials [4, 7, 8]. On the other hand, double-tract (DT) and R-Y pouch reconstructions have been used after total gastrectomy [9]. A prospective randomized controlled trial investigated the differences in body weight, food intake, nutritional conditions, and QOL, determined 3 and 12 months postoperatively, between DT and R-Y reconstructions after total gastrectomy in patients with gastric carcinoma [10]. The trial revealed no advantages of the DT method after total gastrectomy over the simple R-Y method. Thus, various reconstruction methods after total gastrectomy have been considered; however, an optimal method has not been established.

Traditional reconstruction methods to prevent malnutrition and poor QOL after total gastrectomy have focused primarily on the preservation of the duodenal passage and maintaining reservoir capacity. Improving QOL and malnutrition in patients after total gastrectomy may require new insights of intervention. We previously reported that high-resolution impedance manometry (HRIM) helped to evaluate surgical techniques based on the Postgastrectomy Syndrome Assessment Scale-37 (PGSAS-37) in patients who underwent proximal gastrectomy with a hinged double flap [11]. This study aimed to retrospectively investigate whether intraesophageal pressure affects QOL in patients who underwent total gastrectomy with R-Y anastomosis due to postoperative gastric disorders after total gastrectomy.

Material and methods

Twelve patients (nine males and three females) with gastric adenocarcinoma, proven by histopathological findings, underwent total gastrectomy with reconstruction using the R-Y method at Hiroshima University Hospital in Japan between October 2014 and July 2022. The patients were diagnosed with tumor stage according to the seventh edition of the International Union against Cancer tumor-node-metastasis staging system for gastric cancer, and lymph node stations were numbered based on the definitions of the Japanese Gastric Cancer Association [12]. The complications were classified following the Clavien-Dindo classification [13, 14]. Endoscopic assessment of reflux esophagitis was performed according to the Los Angeles classification [15]. This study was approved by the Institutional Review Board of Hiroshima University (No. E2019-1789-03). The study protocol followed the provisions of the Declaration of Helsinki of 1995 (as revised in Brazil, 2013). Written informed consent was obtained from all patients at the initial visit.

Total gastrectomy with D1 + /D2 lymphadenectomy was performed for gastric cancer located in the upper third of the stomach (U region) or for multiple gastric cancers. In all cases, the esophagus was dissected approximately 1 cm above the esophagogastric junction without traction. The esophagogastric junction was defined as the area where the circumference changed from the tubular esophagus to the saccular stomach, as identified via gross observation. Esophagojejunostomy was performed with mechanical staplers (circular stapler and overlap method with linear stapler) and a 40-cm Roux limb. We did not create a large reservoir or neostomach (pouch).

Questionnaire survey

The integrated PGSAS-37 questionnaire was developed by the Japan Postgastrectomy Syndrome Working Party to provide a realistic image of the status of patients who underwent gastrectomy [16, 17]. PGSAS has been frequently used to evaluate postoperative gastrectomy syndrome [18–20]. It comprises 15 items from the Gastrointestinal Symptoms Rating Scale (GSRS) and 22 newly selected items. Therefore, each patient was asked 37 questions.

Case	ECOG-PS	BMI	Operation method	Final TNM	Final stage ^a	Curability	Opening diaphragm	Operation time(min)	Blood loss(ml)	Discharge (POD)	Operative morbidity
-	0	21.6	OTG	T4aN0M0	IIB	RO	(-)	370	4135	16	Grade Illa anastomotic bleeding
2	0	20.7	LTG	T2N2M0	IA	RO	(-)	429	48	12	(-)
ε	0	18.6	OTG	T1bN0M0	IA	RO	(-)	205	29	6	(-)
4	0	23.0	RTG	T1aN0M0	IA	RO	(-)	375	18	12	(-)
5	0	21.4	LTG	T1bN0M0	IA	RO	(-)	245	10	44	Grade II anastomotic leakage
9	0	20.8	OTG	T1aN0M0	IA	RO	(-)	249	106	00	(-)
7	0	19.9	OTG	T1aN0M0	IA	RO	(-)	324	214	46	Grade Illa anastomotic leakage
8	0	22.2	LTG	T1N0M0	IA	RO	(-)	273	41	10	(-)
6	0	18.8	LTG	T1N0M0	Ч	RO	(-)	342	17	11	(-)
10	0	24.8	OTG	T2N0M0	B	RO	(-)	541	705	14	(-)
1	0	28.3	OTG	T3N0M0	ШA	RO	(-)	601	953	11	(-)
12	0	21.9	OTG	T1bN0M0	Ν	RO	(-)	611	285	10	(-)
<i>F</i> femal ^a Stagin	e, <i>M</i> male, <i>ECOG</i> g was performed	Eastern Co d according	operative Oncolo g to the7th editior	gy Group, OTG Op. 1 of the Internation	en total gastrecton nal Union against C	ny, <i>LTG</i> Laparoscc Cancer tumor–no	ppic total gastrector de-metastasis stag	my, <i>RTG</i> Robotic to ing system for gas	otal gastrectomy stric cancer		

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High-resolution impedance manometry

All patients underwent HRIM using the catheter connected to a portable digital recording device (Pocket Monitor GMMS-4000; Starmedical, Inc., Tokyo, Japan). The catheter was inserted nasally under local anesthesia. Ten wet swallows of 5 mL water were administered in the dorsal position during the test, followed by evaluation. The HRIM details have been reported previously [11]. The average maximum intrabolus pressure (IBP; normal value, <17 mmHg), contractile front velocity (CFV; normal value, 2-8 cm/s), distal latency (DL: normal value, >4.5 s), integrated relaxation pressure (IRP; normal value, <15 mmHg), lower esophageal sphincter resting pressure (normal value, 10-45 mmHg), and the LES residual pressure during swallow-induced relaxation (normal value, < 8 mmHg) were evaluated. Postsurgical analysis was performed from 12 to 31 months postoperatively. At the time of the study, there was no evidence of cancer recurrence in all patients.

Statistical analysis

Statistical analyses were performed using JMP (version 10.0.2, SAS Institute Inc., Cary, NC, USA). Unless otherwise indicated, continuous data are expressed as medians and interquartile (25–75th percentiles). Correlations between variables were analyzed using the nonparametric Spearman's rank test. Statistical significance for all tests was set at a two-sided p < 0.05.

Results

Patients' backgrounds

Patient backgrounds and surgical outcomes are listed in Table 1. Twelve patients who underwent total gastrectomy for gastric cancer were included in the study, of whom 25% were female (Table 1). Of the 12 patients (median age: 69.5 years), four underwent laparoscopic total gastrectomy, one underwent robotic total gastrectomy, and seven underwent open total gastrectomy. In laparoscopic and robotic total gastrectomy, esophagojejunostomy was performed by the overlap method using a linear stapler, whereas the reconstruction in open total gastrectomy was performed using a circular stapler. These individuals had a median body mass index of 21.4 kg/m² (range: 18.6-28.3). The median operation time and blood loss were 356 min (range: 205–611 min) and 77 mL (range: 10-4135 mL), respectively. Surgical complications included grade IIIa anastomotic bleeding, grade IIIa anastomotic leakage, and grade II anastomotic leakage in one patient each. The median length of hospital stay was 11.5 days (range, 8-46 days), and there was no recurrence during the 62.4-month median follow-up

period (range 17.6–112.2 months). At 1 year postoperatively, upper gastrointestinal endoscopy revealed reflux esophagitis in three patients.

High-resolution impedance manometry

Postsurgical HRIM analysis was performed at a median of 12.4 months postoperatively. Figure 1 shows the postoperative peristaltic patterns in a representative case. Esophageal peristaltic waves gradually propagate from the upper to the lower esophagus after swallowing. The median of average maximum intrabolus pressure (IBP) was 10.0 (-0.8-25.3) (Fig. 2A). Elevated IBP can be an indirect surrogate marker for an obstructive process at the esophagogastric junction. The median of the CFV was 3.2 (2.0-8.2), and that of the DL was 7.0 (4.8-8.7) (Fig. 2B, C). These indicators of esophageal body motility were almost normal in all patients. The following indicators were used to evaluate the LES function: a certain number of patients with above-normal values for IRP (median: 4.4, -1.2-18.1) and LES residual pressure during swallowing-induced relaxation (median: 5.9, -0.3-18.4), and a certain number of patients with below normal values for LES resting pressure (median: 8.9, 3.9-22.8) (Fig. 2D-F). We compared each parameter between the circular stapler and the overlap method using a linear stapler to determine whether the shape of the anastomosis affects the intraesophageal pressure. There was no significant difference in intraesophageal pressure between the two reconstruction methods (Fig. 3).

Outcome measures in postgastrectomy syndrome assessment scale-37

Table 2 provides a summary of the means and standard deviations of the main outcome measures assessed using the PGSAS-37. We compared our study's data with the Japanese standard data from the PGSAS study using the PGSAS Statistical Kit. The results of this study's PGSAS-37 score were comparable to the Japanese standard data except for the "Dumping subscale" and "Necessity for additional meals."

We next investigated the impact of intraesophageal pressure on postoperative QOL using the correlation between the intraesophageal pressure and PGSAS-37 scores. Among the three indices used to assess LES, higher IRP and LES residual pressure during swallowing-induced relaxation led to better "diarrhea subscale" scores (p=0.0244 and p=0.0244, respectively) (Table 3). In addition, esophageal body motility had an even greater impact on QOL than LES pressure (Table 3). Although the average maximum IBP was not associated with postgastrectomy symptoms, the CFV was involved in the "indigestion subscale," "diarrhea subscale," and "constipation subscale" (p=0.0408, p=0.0143, and



Fig. 1 High-resolution impedance manometry (HRIM) findings. Preoperative and Postoperative high-resolution impedance manometry findings in a representative case. CFV, contractile front velocity; DL, distal latency; IRP, integrated relaxation pressure



Fig. 2 Postoperative assessment at high-resolution impedance manometry. The average maximum intrabolus pressure (A), contractile front velocity (B), distal latency (C), integrated relaxation pressure (D), lower esophageal sphincter (LES) resting pressure (E), and LES residual pressure during a swallowing-induced relaxation (F) for each patient (n = 12). The vertical dashed lines represent the reference normal range



Fig. 3 High-resolution impedance manometry of the patients with circular stapler (n=6) and linear stapler (n=6). C, circular stapler; L, linear stapler. **a**-**f** The average maximum intrabolus pressure (**a**), Contractile front velocity (**b**), Distal latency (**c**), Integrated relaxation pressure (**d**), lower esophageal sphincter (LES) resting pressure (**e**), and LES residual pressure during a swallowing-induced relaxation (**f**) for each patient. Data are presented as the means \pm standard deviation

p = 0.0060, respectively). The distal latency, i.e., the time from upper esophageal sphincter relaxation to the contractile deceleration point, was also associated with the "abdominal pain subscale" (p = 0.0399). Therefore, the results show that HRIM for evaluating intraesophageal pressure is useful for the functional assessment of esophagojejunostomy with R-Y reconstruction after total gastrectomy.

Discussion

Gastric cancer is the third most common cause of cancer deaths worldwide, with 723,000 deaths in 2012 [21, 22]. Recent developments in chemotherapy and the introduction of immune checkpoint inhibitors have improved the clinical outcomes of gastric cancer treatment [23–25]. Consequently, there is an increasing focus on postoperative QOL after gastrectomy, followed by its prognosis.

We previously adopted HRIM to analyze the intraesophageal pressure of esophagogastrostomy using the hinged double flap method after proximal gastrectomy [11]. In patients who underwent esophagogastrostomy using the hinged double flap method, the LES residual pressure during swallowing-induced relaxation was abnormal postoperatively. This is probably due to the resection of the vagus nerves around the LES or the wrapping with gastric sero-muscular flaps, which lead to the lack of swallowing-induced relaxation. In addition, the PGSAS-37 showed that LES residual pressure during the swallowing-induced relaxation and IRP values in HRIM correlated with postgastrectomy syndrome [11]. In the present study, the LES residual pressure during swallowing-induced relaxation and the IRP used to approximate LES relaxation was higher than normal in some patients. The higher-than-normal pressure may be due to the resection of the vagus nerve around the LES

Domain	Item number(#)	Main outcome measures(symptom)	Control	Cases	*р
Symptoms	10, 11, 13, 24	Esophageal reflux subscale	2.0±1.0	1.9±0.8	0.823
	9, 12, 28	Abdominal pain subscale	1.8 ± 0.8	1.4 ± 0.5	0.189
	25-27	Meal-related distress subscale	2.6 ± 1.1	2.1 ± 0.4	0.163
	14–17	Indigestion subscale	2.3 ± 0.9	2.2 ± 0.8	0.768
	19, 20, 22	Diarrhea subscale	2.3 ± 1.2	2.2 ± 0.9	0.856
	18, 21, 23	Constipation subscale	2.1 ± 0.9	1.5 ± 0.4	0.071
	30, 31, 33	Dumping subscale	2.3 ± 1.1	1.5 ± 0.8	0.042
	9–28, 30, 31, 33	Total symptom score	2.2 ± 0.7	1.8 ± 0.5	0.141
Living status	-	Change in body weight (%)	-13.8 ± 7.9	-11.8 ± 9.8	0.491
	34	Ingested amount of food per meal	6.4 ± 1.9	5.9 ± 1.4	0.433
	41	Necessity for additional meals	2.4 ± 0.8	2.9 ± 1.2	0.045
	38–40	Quality of ingestion subscale	3.8 ± 0.9	3.7 ± 0.6	0.855
	42	Ability for working	2.0 ± 0.9	2.5 ± 0.7	0.153
QOL	43	Dissatisfaction with symptoms	2.1 ± 1.0	2.3 ± 1.1	0.55
	44	Dissatisfaction at the meal	2.8 ± 1.1	2.5 ± 1.3	0.435
	45	Dissatisfaction at working	2.1 ± 1.1	2.3 ± 0.7	0.671
	43–45	Dissatisfaction for daily life subscale	2.3 ± 0.9	2.3 ± 0.9	0.877

 Table 2
 Scores of the PGSAS-37 symptom at 1 year after surgery

* Comparison between the data of total gastrectomy (n = 8) with the values of the Japanese standard data of the PGSAS study using the PGSAS statistic kit

in total gastrectomy as well as in proximal gastrectomy. In addition, as in our previous study, LES residual pressure and IRP values affected postgastrectomy syndrome in this study. Intraesophageal pressure at the reconstruction site after gastrectomy may have different normal values than preoperatively. In contrast, some patients had a lower-than-normal LES resting pressure, probably because of the relatively large diameter without a flap. LES resting pressure with R-Y reconstruction did not correlate with postgastrectomy syndrome, similar to proximal gastrectomy. It is plausible that LES residual pressure during swallowing-induced relaxation and IRP, which occurs after swallowing, were more involved in postgastrectomy syndrome than the LES resting pressure. We then analyzed the average values of intraesophageal pressure of the patients suffering from anastomotic leakage after surgery. Although statistical analysis was not possible due to the small number of patients with anastomotic leakage (only two), IRP and LES residual pressure were lower (data not shown). Further analysis is needed to determine whether anastomotic leakage is associated with postgastrectomy syndrome due to lower IRP and LES residual pressure.

Conversely, esophageal peristalsis influenced postgastrectomy symptoms in the present study, in contrast to what was observed in patients who underwent proximal gastrectomy. Among the three indices used to assess esophageal peristalsis, CFV correlated with the three PGSAS-37 subscales, indicating that the peristaltic velocity of the esophagus was the most crucial factor for postgastrectomy syndrome. The higher the CFV and the lower the DL, the more pronounced the postgastrectomy symptoms. Patients who undergo R-Y reconstruction may be susceptible to esophageal peristalsis because the small intestine has no reservoir function in total gastrectomy. In contrast, since the esophagus is anastomosed to the residual stomach in proximal gastrectomy, patients who undergo proximal gastrectomy may be less susceptible to esophageal peristalsis [11]. However, we can only speculate and discuss this issue based on the data in this study. Unfortunately, the involvement of intraesophageal pressure in each of the postgastrectomy symptoms after gastrectomy cannot be adequately explained by this study. Since the esophagus is only a small part of the gastrointestinal tract, and postgastrectomy syndrome is related to various factors such as the sympathetic nervous system, blood flow in the gastrointestinal tract, hormones, intestinal bacteria, etc., this requires further investigation.

Two stapler types are commonly used in esophagojejunostomy with R-Y reconstruction: linear stapler and circular stapler [26]. The overlap method was first reported as a side-to-side anastomosis of the jejunum to the esophagus using a linear stapler in an isoperistaltic direction; it is now a leading procedure in intracorporeal anastomosis due to the easy insertion of an instrument into the esophageal stump [27, 28]. This procedure was expected to eliminate anastomotic leakage due to watertight triple-layer stapling, avoid anastomotic bleeding, and secure a wide diameter [28, 29]. Based on

	Integrate pressure	d relaxation	LES restin	ig pressure	LES residu	ual pressure	intrabolu	s pressure	contractil velocity	e front	distal late	ncy
	٩	*p value	٩	*p value	٩	* <i>p</i> value	٩	*p value	٩	*p value	٩	* <i>p</i> value
Esophageal reflux subscale	0.1687	0.690	-0.0602	0.887	0.1687	0.690	-0.3133	0.450	-0.2546	0.582	-0.3819	0.398
Abdominal pain subscale	0.0128	0.976	-0.0383	0.928	0.0128	0.976	-0.1788	0.672	0.0996	0.832	-0.7769	0.040
Meal-related distress subscale	-0.0124	0.977	-0.2224	0.597	-0.0124	0.977	-0.3706	0.366	-0.0748	0.873	0.3555	0.434
Indigestion subscale	-0.6386	0.088	-0.1566	0.711	-0.6386	0.088	-0.0482	0.910	0.7748	0.041	-0.4144	0.355
Diarrhea subscale	-0.7734	0.024	-0.4174	0.304	-0.7734	0.024	-0.2701	0.518	0.8547	0.014	-0.2000	0.667
Constipation subscale	-0.6054	0.112	-0.4942	0.213	-0.6054	0.112	-0.2841	0.495	0.8982	0.006	0.0561	0.905
Dumping subscale	-0.3856	0.346	0.2289	0.586	-0.3856	0.346	0.0482	0.910	0.3637	0.423	-0.0727	0.877
Total symptom score	-0.5476	0.160	-0.2143	0.610	-0.5476	0.160	-0.2143	0.610	0.6786	0.094	-0.4286	0.337

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су а ty, a e) B 5 e, I 5 ے نو וקט ц С 5 Association Detween the six indices, integrated relaxation of PGSAS-37 (n = 8). LES lower esophageal sphincter a retrospective study, Kawamura et al. recommended overlap esophagojejunostomy using a linear stapler due to the reduced incidence of anastomotic complications compared with a circular stapler [29]. Hence, we compared the HRIM data of the two methods for total gastrectomy regarding esophageal pressure. Contrary to our expectation, the three indicators used to evaluate LES function were not statistically different in patients with the linear stapler compared to those with the circular stapler, but the median values of the LES residual pressure and LES resting pressure tended to be lower in patients with the linear stapler, which may have been influenced by the larger anastomotic diameter of the linear stapler. A detailed comparison of the superiority of the two reconstruction methods in total gastrectomy using HRIM will require further case accumulation.

Nearly total gastrectomy with preservation of the vagus nerve and the LES was developed as a functionpreserving surgical technique to improve postgastrectomy disorders [30, 31] In this study, total gastrectomy was performed for tumors located in the upper third of the stomach (U region) or for multiple tumors, but not for esophagogastric junction cancer. Therefore, although the exact distance between the vagus nerve cut and the esophageal stump was not measured, the esophagus was dissected at 1 cm above the esophago-gastric junction in all cases and the distance was not very different in each case. In gastrectomy for esophagogastric junction cancer, which is currently increasing worldwide, the distance varies widely from case to case. The impact of this distance on LES function and postoperative symptoms is a subject for future study. The present study has some other limitations, which include using data from a single institution, failure to take into account the deterioration in esophageal function due to aging, its retrospective design, evaluating only two reconstruction methods, and a small sample size.

Conclusions

This literature is noteworthy that it is the first to objectively demonstrate the association between intraesophageal pressure of R-Y reconstruction and postoperative QOL in patients undergoing total gastrectomy. The present study elucidated HRIM as an evaluation method for surgical procedures. This will lead to the development of new surgical procedures to improve QOL.

Abbreviations

HRIM	High-resolution impedance manometry
R-Y	Roux-en-Y
PGSAS-37	Postgastrectomy Syndrome Assessment Scale-37
LES	Lower esophageal sphincter
QOL	Quality of life
DT	Double-tract
GSRS	Gastrointestinal Symptoms Rating Scale

- CFV Contractile front velocity
- DL Distal latency
- IRP Integrated relaxation pressure

Authors' contributions

Y.S. designed and analyzed the data and wrote the manuscript; K.T., O.M., E.T., and N.K. edited the manuscript; E.C., H.O., Y.T., N.K., and A.K. performed HRIM; H.O. supervised the project. All authors reviewed the manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Hiroshima University (No. E2019-1789–03). The study protocol followed the provisions of the Declaration of Helsinki of 1995 (as revised in Brazil, 2013). Written informed consent was obtained from all patients at the initial visit.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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