Surgical Endoscopy (2018) 32:4277–4283
https://doi.org/10.1007/s00464-018-6177-1

Safety and curability of laparoscopic gastrectomy in elderly patients with gastric cancer

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Received: 15 October 2017 / Accepted: 21 March 2018 / Published online: 30 March 2018

Abstract

Background Elderly patients are often considered as a high-risk population for major abdominal surgery due to reduced functional reserve and increased comorbidities. The aim of this study was to assess the safety and curability of laparoscopic gastrectomy in elderly patients with gastric cancer compared with short- and long-term outcomes in non-elderly patients.

Methods We retrospectively investigated 386 patients who underwent laparoscopic gastrectomy for gastric cancer between January 2007 and December 2015 at the Digestive Disease Center, Showa University, Northern Yokohama Hospital. We categorized the patients into two groups by age: the elderly patients (≥ 75 years old) and the non-elderly patients (< 74 years old). Patient characteristics, clinicopathologic and operative findings, and short- and long-term outcomes were investigated and compared between the two groups.

Results The elderly group showed a significantly higher rate of comorbidities (73.1 vs. 49.2%, $P < 0.001$), and American Society of Anesthesiologists (ASA) scores ≥ 2 (76.3 vs. 43.7%, $P < 0.001$), and using anticoagulant agents (25.8 vs. 7.9%, $P < 0.001$) than the non-elderly group. The postoperative morbidity and mortality did not differ between the two groups (19.4 vs. 18.8%; $P = 0.880$, 2.2 vs. 0%; $P = 0.058$). In the multivariate analysis, male sex was the only risk factor for postoperative morbidity after laparoscopic gastrectomy. However, age was not found to be a risk factor. The 5-year overall survival ratio was significantly lower in the elderly group than in the non-elderly group (67.7 vs. 85.0%; $P < 0.001$). However, the 5-year disease-specific survival ratio was similar in the two groups (84.8 vs. 89.1%; $P = 0.071$).

Conclusion Laparoscopic gastrectomy for gastric cancer could be safely performed in elderly patients with acceptable postoperative morbidity and curability.

Keywords Laparoscopic gastrectomy · Elderly patients · Gastric cancer

Although the incidence of gastric cancer is decreasing in most part of the world, gastric cancer is currently the second most common cause of death from malignant disease in Japan [1]. Notably, the world population is rapidly aging as life expectancies rise. Approximately 60% of cancer incidence and 70% of cancer-related mortalities occur in individuals over the age of 65 years [2]. Thus, surgical treatment for elderly patients with gastric cancer will become essential. However, appropriate decisions regarding the surgical course in elderly patients are difficult to make primarily because elderly patients are often considered as a high-risk population for major abdominal surgery due to reduced functional reserve and increased comorbidities. An optimal treatment decision in the elderly in terms of operative approach or extent of surgery warrants caution to balance safety and curative impact.

Since the first reported laparoscopic distal gastrectomy for gastric cancer in 1994 [3], several studies have demonstrated the clinical advantages of laparoscopic surgery over open surgery [4–7]. The advantages include reductions in morbidity rate, pain, and duration of postoperative hospital stay, and a faster recovery [8, 9]. Furthermore, several studies have investigated the feasibility of laparoscopic gastrectomy in elderly patients [10–15]. However, the feasibility of laparoscopic gastrectomy in elderly patients is still controversial.

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The aim of this study was to assess the safety and curability of laparoscopic gastrectomy in elderly patients with gastric cancer compared with the short- and long-term outcomes in the non-elderly patients.

Patients and methods

Study design and study setting

A retrospective study design was used to enroll eligible patients at the Digestive Disease Center, Showa University, Northern Yokohama Hospital.

Patients

A total of 386 patients who underwent laparoscopic gastrectomy for gastric cancer between January 2007 and December 2015 were enrolled in this study. We categorized the patients into two groups by age: elderly (≥ 75 years old) and non-elderly (< 74 years old). Patient characteristics, clinicopathological findings, and short-term outcomes were investigated and compared between the two groups. Furthermore, long-term outcomes were also compared between the two groups. In the present study, comorbidities were classified as eight groups: hypertension, cardiovascular disease, pulmonary disease, cerebrovascular disease, diabetes mellitus, liver disease, renal disease, and other diseases. The clinicopathological findings of the patients were evaluated based on the Japanese Classification of Gastric Carcinoma (3rd English edition) published by the Japanese Gastric Cancer Association (JGCA) [16]. The inclusion criteria for this study were as follows: curative dissection, pathologically confirmed gastric adenocarcinoma, a R0 resection, no evidence of distant metastasis, and no adjuvant chemotherapy prior to surgery. Short-term outcomes (defined as complications or death within 30 days of surgery or during hospital stay) were investigated by evaluating the postoperative morbidity, mortality, and hospital stay. For standardization purposes, complications were classified according to the Clavien–Dindo classification system [17]. Clavien–Dindo Grade 2 or higher was defined as complication. Long-term outcomes were evaluated by comparing the overall and the disease-specific survival ratio between the two groups.

Surgical procedure

Each patient was placed in the supine position under general anesthetic; the operator stood on the right side of the patient, the assistant stood on the left of the patient, and endoscopist stood between the patient's legs. Initially, a 12-mm trocar (for a 30° rigid electrolaparoscope) was inserted through a umbilical incision using the open technique. After we established pneumoperitoneum with carbon dioxide, four additional trocars were introduced into the right upper quadrant (5 mm), right middle quadrant (12 mm), left middle quadrant (5 mm), and left upper quadrant (12 mm) region of the abdomen. A Nathanson liver retractor was inserted in the upper mid-abdomen for liver traction. And pneumoperitoneum was maintained at 12 mmHg during the surgery. The extent of resection was determined by the location of the primary tumor and the lymph node status. By using Laparoscopic Coagulating Shears, we performed mainly D1 plus lymphadenectomy for early gastric cancer; however, we based this on Japanese Classification of Gastric Carcinoma (3rd English edition) published by the Japanese Gastric Cancer Association [12]. D2 lymphadenectomy was performed in patients with advanced gastric cancer. After these procedures, Roux-en-Y gastrojejunostomy was performed using an intracorporeal approach that included Linear stapling devices. In case of total gastrectomy, esophagojejunostomy was usually performed with a circular stapler and transorally inserted anvil (Orvil, Coviden, Mansfield, MA, USA).

Patient follow-up

After the surgery, patients were managed with standardized clinical protocols. Nasogastric tube placement was not routinely performed. Intravenous or epidural anesthesia was used for postoperative pain control. Patients started an oral diet on postoperative day (POD) 3 or 4. If the patient had no complication, or other medical problems, the patient was discharged on POD 9–12. Adjuvant chemotherapy was initiated in patients with stage II or III cancer. All patients were regularly followed for at least 3 years after surgery. Follow-up investigations were scheduled at 3-month intervals for the first 2 years, at 6-month intervals for the next 3 years, and then annually until the death of the patient.

Statistical analysis

Data were analyzed using JMP Pro 12 ® (SAS Institute Inc. Cary, NC, USA). For comparison between the two groups, the Chi-square test or Fisher's exact was used for categorical variables as appropriate, and Student's *t* test was used for continuous variables. Continuous variables were expressed as the mean ± standard deviation (SD), while the categorical variables were expressed as frequency as percentages. The cumulative survival time was calculated by the Kaplan–Meier method and the log-rank test. To elucidate the risk factors of postoperative complication and the prognostic factors indicating disease recurrence, multivariate analysis was performed. Probability (*P*) values were considered to be statistically significant at $P < 0.05$ level.

Results

Characteristics and clinicopathological findings

Table 1 shows the characteristics and clinicopathological findings of the two groups. The elderly group consisted of 93 (24.1%) patients and the non-elderly group, 293 (75.9%) patients. The mean age in the elderly group was 78 ± 6.2 years, with majority being male (73.1%). Among the elderly, 68 (73.1%) had underlying comorbidities, and 30 (32.6%) had a history of abdominal surgery. The mean body mass index (BMI) was 22.3 ± 3.2 kg/m^2. Twenty-four patients (25.8%) used anticoagulant agents. The elderly group showed a significantly higher rate of comorbidities (73.1 vs. 49.2%, $P < 0.001$) and ASA scores ≥ 2 (76.3 vs. 43.7%, $P < 0.001$), and using anticoagulant agents (25.8 vs. 7.9%, $P < 0.001$) than the non-elderly group, whereas no significant differences were observed in terms of sex, BMI, and history of abdominal surgery between the two groups. Further there are no significant differences in tumor size, depth of invasion, N classification, pathologic stage, or the administration of adjuvant treatment between the two groups.

Operative findings and short-term outcomes

Table 2 shows operative findings for the two groups. In the elderly group, there were 23 (23.8%) cases of the total gastrectomy, mean operation time was 250 ± 63.9 min, and the mean intraoperative blood loss was 70 ± 123.8 ml. Compared with the non-elderly group, there were no significant differences in the operation method, operation time, blood loss. However, in the elderly group, the frequency of D2 dissection (19.6 vs. 37.5%, $P = 0.011$) was significantly lower, while the mean number of retrieved lymph nodes (44 ± 24.3 vs. 54 ± 27.7, $P < 0.001$) was fewer compared with the non-elderly group.

After surgery, there were no significant differences in postoperative morbidity (19.4 vs. 18.8%; $P = 0.880$) and mortality (2.2 vs. 0%; $P = 0.058$), time to oral intake (4 ± 3.4 vs. 4 ± 5.0 days; $P = 0.603$), and postoperative hospital stay (9 ± 7.5 vs. 9 ± 9.5 days; $P = 0.903$). Two patients (2.2%) died of intraabdominal bleeding in the elderly group (Table 3).

Long-term outcomes

The median follow-up period for all patients was 36 (range 1–108) months. There is no significant discrepancy in follow-up period between the two groups (32 ± 22.1 vs. 36 ± 21.1 month; $P = 0.067$), and the 5-year overall survival ratio was significantly lower in the elderly group than in the non-elderly group (67.7 vs. 85.0%; $P < 0.001$, Fig. 1). However, the 5-year disease-specific survival ratio was similar in the two groups (84.8 vs. 89.1%; $P = 0.071$, Fig. 2).

Discussion

Elderly patients are often considered as a high-risk population for major abdominal surgery due to reduced functional reserve and increased comorbidities. However, laparoscopic gastrectomy has recently become widely accepted as a therapeutic option for gastric cancer due to its superiority to open surgery, including decreased blood loss, reduced pain, fewer postoperative complications, and shorter hospital stay [3–9, 18]. When considering the trauma induced by surgery, laparoscopic surgery may be optimal for minimizing surgical trauma in elderly patients. Recently several studies on laparoscopic gastrectomy in the elderly gastric cancer patients have been published; however, most of these studies focused on distal gastrectomy and short-term outcomes [10–15, 19]. Therefore, the safety and curability of laparoscopic gastrectomy in elderly patients with gastric cancer including cases with total gastrectomy remains unclear. In this retrospective study, we investigated and compared patient characteristics, clinicopathologic and operative findings, as well as short- and long-term outcomes between elderly and non-elderly patients treated with laparoscopic gastrectomy for gastric cancer. Studies of gastric cancer surgery in elderly patients were based on several different age criteria: the commonly defined ages for the elderly were ≥ 70 years [15, 19], ≥ 75 years [20, 21], and ≥ 80 years [22, 23]. Kurian et al. [24] reported that the mortality risk for major gastrointestinal resections increased very rapidly at 75 years of age; therefore, in this study, we designated patients aged ≥ 75 years as "elderly" group. Generally, elderly patients are more likely to have comorbidities such as cardiopulmonary disease, hypertension, cerebrovascular disease, and renal disease which may be associated with postoperative morbidity [25]. In this study, although elderly patients were more likely to have a poor ASA and comorbidities, postoperative morbidity was similar between the two groups (elderly group vs. non-elderly group: 19.4 vs. 18.8%; $P = 0.880$). There are several possible explanations for this result. The first may be due to the careful pre- and postoperative management concerning organ function and performance status. The second is the influence of limited lymph node dissections performed frequently in the elderly group. Elderly patients were more likely to performed limited lymph nodes dissection. It may due to regarding organ function and performance status of the elderly patients. If grossly enlarged lymph nodes were detected at any particular D2 area, our operators mandatorily perform complete D2 dissection for curative intent. However, if enlarged lymph

Table 1 Patient characteristics

Variables	Elderly ($n=93$)	Non-elderly ($n=293$)	P value
Age (years)	78 ± 6.2	65 ± 10.4	< 0.001
Sex (male) [n (%)]	68 (73.1)	214 (73.0)	0.552
BMI (kg/m^2)	22.7 ± 2.9	22.3 ± 3.2	0.299
ASA score [n (%)]			< 0.001
1	22 (23.7)	165 (56.3)	
2	54 (58.1)	102 (34.8)	
3	17 (18.2)	26 (8.9)	
Comorbidity [n (%)]	39 (70.1)	105 (55.9)	< 0.001
Hypertension	48 (51.6)	91 (31.1)	< 0.001
Cardiovascular disease	17 (18.3)	21 (7.2)	< 0.001
Pulmonary disease	26 (28.0)	41 (14.0)	0.003
Cerebrovascular disease	16 (17.2)	15 (5.1)	< 0.001
Diabetes mellitus	21 (22.6)	47 (16.0)	0.161
Liver disease	1 (1.1)	5 (1.7)	0.555
Renal disease	6 (6.5)	3 (1.0)	0.008
Other	2 (2.2)	5 (1.7)	0.676
History of abdominal surgery [n (%)]	30 (32.6)	69 (23.6)	0.101
Using anticoagulant agents [n (%)]	24 (25.8)	23 (7.9)	< 0.001
Histologic type [n (%)]			< 0.001
Differentiated	63 (67.7)	128 (43.7)	
Undifferentiated	30 (32.3)	165 (56.3)	
Tumor size (mm)	35 ± 26.5	35 ± 26.2	0.358
Depth of tumor [n (%)]			0.297
T1a (mucosa)	20 (21.5)	92 (31.4)	
T1b (submucosa)	45 (48.4)	108 (36.9)	
T2 (muscularis propria)	10 (10.7)	41 (14.0)	
T3 (subserosa)	13 (14.0)	37 (12.6)	
T4a (invade serosa)	5 (5.4)	14 (4.8)	
T4b (invade adjacent structures)	0 (0)	1 (0.3)	
N classification [n (%)]			0.431
N0	65 (69.9)	223 (76.1)	
N1	11 (11.8)	36 (12.3)	
N2	8 (8.6)	14 (4.8)	
N3	9 (9.7)	20 (6.8)	
Pathologic stage [n (%)]			0.759
IA	56 (60.2)	181 (61.8)	
IB	11 (11.8)	41 (14.0)	
IIA	8 (8.6)	29 (9.9)	
IIB	6 (6.5)	11 (3.8)	
IIIA	3 (3.2)	8 (2.7)	
IIIB	5 (5.4)	18 (6.1)	
IIIC	4 (4.3)	5 (1.7)	
Adjuvant treatment [n (%)]			0.175
Yes	13 (14.3)	61 (20.9)	
No	78 (85.7)	231 (79.1)	

Values are expressed as means ± standard deviation (SD), or n (%)

BMI body mass index, *ASA* American society of Anesthesiologists

Table 2 Operative findings

Variables	Elderly ($n=93$)	Non-elderly ($n=293$)	P value
Operation method [n (%)]			0.889
Total gastrectomy	23 (23.8)	69 (23.6)	
Distal gastrectomy	70 (76.2)	224 (76.4)	
Operation time (min)	250 ± 63.9	260 ± 51.7	0.183
Blood loss (ml)	70 ± 123.8	80 ± 102.4	0.854
Lymph node dissection [n (%)]			< 0.001
D1/D1+	74 (80.4)	183 (62.5)	
D2	18 (19.6)	11 (37.5)	
Number of retrieved Lymph nodes	44 ± 24.3	54 ± 27.7	0.007

Values are expressed as means ± standard deviation (SD), or n (%)

Table 3 Short-term outcomes

Variables	Elderly ($n=93$)	Non-elderly ($n=293$)	P value
Morbidity [n (%)]	18 (19.4)	55 (18.8)	0.880
Wound infection	0 (0)	2 (0.7)	0.576
Pancreatic fistula	0 (0)	4 (1.4)	0.330
Anastomotic leakage	2 (2.1)	3 (1.0)	0.348
Hemorrhage/hematoma	6 (6.5)	8 (2.7)	0.092
Anastomotic stenosis	2 (2.1)	5 (1.7)	0.534
Intraabdominal abscess	3 (3.2)	14 (4.8)	0.382
Delayed gastric emptying	2 (2.1)	8 (2.7)	0.552
Ileus	0 (0)	3 (1.0)	0.436
Cardiovascular	0 (0)	1 (0.3)	0.759
Pneumonia/atelectasis	0 (0)	2 (0.7)	0.576
Others	3 (3.2)	5 (1.7)	0.298
Mortality [n (%)]	2 (2.1)	0 (0)	0.424
Time to oral intake (days)	4 ± 4.0	4 ± 3.4	0.795
Postoperative hospital stay (days)	9 ± 9.5	9 ± 7.5	0.253

Data are expressed as mean ± standard deviation (SD), or n (%)

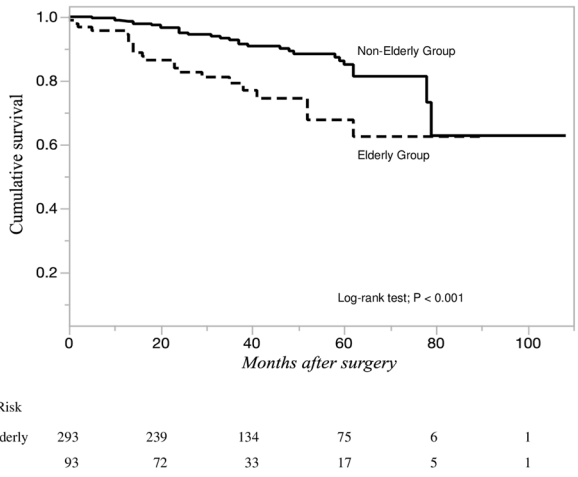

Fig. 1 5-year overall survival

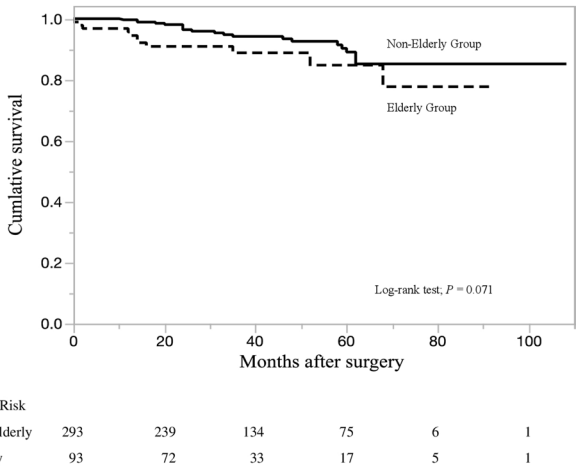

Fig. 2 5-year disease-specific survival

nodes are not detected, or are only restricted to D1area, less complete D2 dissection might be performed at the operator's own discretion in frail elderly patients. The rate of postoperative hemorrhage or hematoma was higher in the elderly group, probably because the large number of anticoagulant users in this group may lead to this result. The postoperative mortality rate, time to oral intake, and duration of postoperative hospital stay did not significantly differ between the two groups, and on multivariate analysis, only male sex was identified as an independent risk factor for postoperative morbidity (Table 4). The finding reveals that age is not a risk factor for postoperative morbidity. This suggests that the short-term outcomes of laparoscopic gastrectomy are the same in the elderly and the non-elderly patients. Furthermore, laparoscopic gastrectomy can be performed safely in the elderly patients by careful pre- and postoperative management concerning organ function and performance status. And it might be necessary to refrain lymph node dissection according to the risk factor.

Regarding oncologic outcomes, disease-specific survival ratio was similar in both elderly group and the non-elderly

Table 4 Univariate and multivariate analysis of risk factors for postoperative complication

Variables	Univariate analysis	Multivariate analysis		
	P value	Odds ratio	95% CI	*P* value
Gender (male)	0.028	2.131	1.065–4.264	0.033
Age (< 75 vs. ≥ 75 years)	0.880	1.136	0.606–2.133	0.690
BMI (< 25 vs. ≥ 25)	0.876	1.272	0.657–2.465	0.475
Comorbidity	0.299	1.150	0.660–2.002	0.622
Operation method Total vs. distal gastrectomy	0.879	1.079	0.571–2.040	0.814
Lymph node dissection D1/D1+ vs. D2	0.073	1.655	0.956–2.867	0.072
Operation time (≥ 300 min)	0.100	1.469	0.815–2.646	0.201
Blood loss (≥ 150 ml)	0.098	1.438	0.785–2.632	0.240

CI confidence interval

group; however, the overall survival ratio was significantly lower in the elderly group than in the non-elderly group. Elderly patients died of other causes than gastric cancer during follow-up. In the present study, there were 10 patients of death not related to gastric cancer in the elderly group. The main causes of death in their follow-up periods were pneumonia (30.0%) and die of old age (30.0%) and cerebral infarction (10.0%). Especially death within 1 year after surgery was 1 patient in the elderly group and 1 patient in the non-elderly group, both of which caused by pneumonia. Therefore, there are no significant differences of ratio of deaths within 1 year after surgery between the two groups (elderly group vs. non-elderly group: 1.1 vs. 0.34%; $P = 0.424$). Although, limited lymph node dissections were frequently performed in the elderly group, as shown in Table 2, apparently, limited lymph node dissection did not seem to have had an influence on the disease-specific survival in the elderly patients. This result might be due to the differences in tumor growth and metastatic potential in both elderly patients and the non-elderly patients. Furthermore, Tokunaga et al. and Jiang et al. [26, 27] revealed that postoperative intraabdominal infectious complications and higher grade of complications according to the Clavien–Dindo classifications were strongly associated with poor overall survival time and relapse-free survival time. In this study, recurrence ratio was similar between the two groups (elderly group vs. non-elderly group: 8.79 vs. 7.88%; $P = 0.826$). Moreover, the frequency of Clavien–Dindo Grade 3 or higher postoperative morbidities were also equal in the two groups (elderly group vs. non-elderly group: 9.68 vs. 9.56%; $P = 0.603$). We performed univariate and multivariate analysis to investigate risk factors for postoperative recurrence after laparoscopic gastrectomy (Table 5). Depth of tumor ≥ T2, 3, and N classification ≥ N2, 3, and absence of adjuvant treatment were identified as independent risk factors for recurrence. However, lymph node dissection and age were not independent risk factor. The odds ratio of the patients with Clavien–Dindo Grade 3 or higher postoperative morbidities was slightly high (odds ratio 3.335, 95% CI 0.966–11.515, $P = 0.057$). This result suggests that appropriate lymph node dissection might be necessary, but meticulous surgery and to prevent perioperative complications are needed to improve the long-term outcomes of patients following curative gastrectomy.

The limitations of our study included its retrospective design and that it was limited to a single institution.

Table 5 Univariate and multivariate analysis of risk factors for postoperative recurrence

Variables	Univariate analysis	Multivariate analysis		
	P value	Odds ratio	95% CI	*P* value
Gender (male)	0.021	3.332	0.852–12.924	0.084
Age (< 75 vs. ≥ 75 years)	0.826	1.140	0.396–3.282	0.808
Morbidity (C–D > 3)	0.509	3.335	0.966–11.515	0.057
Lymph node dissection D1/D1+ vs. D2	0.167	1.332	0.511–3.476	0.558
T1, 2 or T3, 4	< 0.001	4.253	1.302–13.880	0.017
N0, 1 or N2, 3	< 0.001	3.858	1.244–11.960	0.019
Adjuvant treatment (no)	< 0.001	3.847	1.140–12.913	0.030

C–D Clavien–Dindo Grade, *CI* confidence interval

In conclusion, laparoscopic gastrectomy for gastric cancer could be safely performed in elderly patients with an acceptable postoperative morbidity and curability. The findings of this study could be used in the development of appropriate guidelines for the management of elderly patients with gastric cancer to enhance the quality of life. Further investigations using a prospective cohort study design are needed to confirm the effect of age on short- and long-term outcomes of laparoscopic gastrectomy for gastric cancer patients.

Compliance with ethical standards

Disclosures Shoji Shimada, Naruhiko Sawada, Sonoko Oae, Junichi Seki, Yojiro Takano, Yasuhiro Ishiyama, Kenta Nakahara, Chiyo Maeda, Eiji Hidaka, Fumio Ishida, Shin-ei Kudo declares that they have no conflicts of interest or financial ties to disclose.

Ethical approval This study was approved by Showa University Northern Yokohama Hospital ethics committee and all the patients.

Informed consent For this type of retrospective study formal consent is not required.

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