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Short-Term and Long-Term Outcomes After Gastrectomy for Gastric Cancer in Patients With Chronic Kidney Disease

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Abstract

Background The incidence of chronic kidney disease (CKD) is increasing, which might be an obstacle to various aspects of gastric cancer treatment, such as perisurgical management and postsurgical follow-up. The present study aimed to evaluate the short- and long-term surgical outcomes following gastrectomy in patients with CKD.

Methods We retrospectively analyzed surgical complications and prognosis of patients with gastric cancer. These patients were divided into three groups according to the glomerular filtration rate (GFR): 49 patients with severe CKD (GFR < 29 ml/min/1.73 m^2), 128 with mild CKD (GFR 30–59), and 798 in the controls (GFR ≥ 60).

Results The incidences of anastomotic leakage and intraabdominal abscess in the mild and severe CKD groups were higher than that in the control group. The incidences of wound infection, cardiovascular and pulmonary events, and in-hospital mortality in the severe CKD group were higher than those in the other two groups. Severe surgical complications were associated with co-morbidities other than CKD, serum albumin level, estimated blood loss, surgery duration in the mild and severe CKD group. The 3-year overall survival rates for the severe CKD, mild CKD, and control groups were 48.6, 80.9, and 85.0 %, respectively, indicating significant differences between the severe CKD group and other two groups.

Conclusions Patients with severe CKD show an increased risk of morbidity and mortality following gastrectomy, and their prognosis is usually poor. Studies with a large cohort are essential to refine the risk stratification for gastrectomy in this high-risk population.

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Introduction

The incidence of renal disease, chronic kidney disease (CKD) in particular, is increasing as the population worldwide is aging [1, 2]. Several studies have reported that patients with CKD experience a high incidence of malignant tumors [3, 4]. Although advances in surgical techniques and perioperative management have made it possible to perform gastrectomy safely, renal dysfunction remains a major risk factor because it is related not only to the metabolic and coagulopathic disorders secondary to uremia and anuria but also to other co-morbidities [5, 6]. Nonetheless, there remains a lack of detailed data on the impact of CKD during perioperative gastrectomy. In addition, the prognosis of patients with CKD undergoing gastrectomy is unclear. The present retrospective study evaluated the short- and long-term outcomes after gastrectomy in patients with CKD versus those with normal renal function and no co-morbidity.

Patients and methods

The subjects were patients with primary gastric cancer (GC) without distant organ metastases who underwent elective, potentially curative surgery at Nara Medical University Hospital (Nara, Japan) between January 1997 and December 2011. Patients whose records documented any of the following conditions were excluded: microscopic (R1) and macroscopic (R2) incomplete resection or advanced cancer in another organ.

Renal function was assessed by calculating the glomerular filtration rate (GFR) from serum creatinine (sCr) levels using the latest Japanese coefficient for Modification of Diet in Renal Disease formula [eGFR (ml/min/1.73 m^2) = 194 × $sCr^{-1.094}$ × $age^{-0.287}$ × 0.739 (for female patients)] [7]. CKD stage was categorized using the Kidney Disease: Improving Global Outcomes (KDIGO) classification system [8], which categorizes GFR in the following ranges: stage 3, 30–59 ml/min/1.73 m^2; stage 4, 15–29 ml/min/1.73 m^2; stage 5, <15 ml/min/1.73 m^2. In this study, stages 4 and 5 CKD were defined as severe and stage 3 as mild. As a control group, we enrolled patients undergoing gastrectomy with normal renal function (GFR >60 ml/min/1.73 m^2).

The clinicopathologic findings were determined according to the criteria for Japanese Classification of Gastric Carcinoma [9]. The extent of lymph node (LN) dissection was determined on the basis of the Japanese Gastric Cancer Treatment Guidelines 2010 (version 3) [10]. In this study, D1 LN dissection included D1 and D1 + LN dissections.

Surgery

Patients diagnosed with early GC located in the upper and middle thirds of the stomach without LN involvement underwent proximal gastrectomy and pylorus-preserving gastrectomy (PPG), respectively. The choice of surgical procedure, total or proximal gastrectomy and distal gastrectomy or PPG, was at the discretion of the surgeons and patients. In general, D1 gastrectomy was performed for cT1 disease and D2 gastrectomy for cT2–cT4 disease in this study. However, despite advanced cancers, D1 gastrectomy was adopted for elderly patients or those with severe renal dysfunction, as determined by the surgeon.

Surgical complications

Surgical complications were determined from patient records during hospitalization and within 30 days after surgery and were then stratified according to the Clavien–Dindo (CD) classification [11]. If more than one complication occurred in a single patient, the most severe one was recorded. Although the CD classification is categorized by surgical complications graded I through V, grade I was not evaluated to exclude the possibility of description bias in patient records. Pulmonary complications after gastrectomy included pneumonia, pleural effusion, and pulmonary edema. Cardiovascular complications included cardiac diseases, such as arrhythmia, angina pectoris, myocardial infarction, congestive heart failure, and peripheral vessel diseases (e.g., deep vein thrombosis).

Statistical analysis

Continuous variables, presented as means, were compared using the Student's t test or one-way analysis of variance, and post-hoc multiple comparison analysis performed using Tukey's or the Games–Howell procedure. In addition, Pearson's χ^2 test or Fisher's exact test was used for analysis of categoric data. The survival outcome used for this study was overall survival (OS), which was calculated from the time of surgery. We estimated the OS rate using the Kaplan–Meier method. Statistical analysis was performed using the log-rank test. A multivariate analysis was performed using the Cox's proportional hazards model to evaluate independent prognostic factors. Variables that were found to be significant on univariate analysis at $p < 0.05$ were included in the multivariate analysis. Age was evaluated as a continuous variable and included in the univariate and multivariate analyses. For all tests, a $p < 0.05$ was considered statistically significant. All analyses were performed using SPSS statistical software (SPSS, Chicago, IL, USA).

Results

The baseline patient characteristics are presented in Table 1. There were 49 patients in the severe CKD group (21 with maintenance hemodialysis), 128 in the mild CKD group, and 798 in the control group. Patients in the severe and mild CKD groups were significantly older than those in the control group, and the frequency of co-morbidity other than CKD was higher in these two groups than in the control group. Tumor staging was similar among the three groups. Progression of CKD was associated with anemia. The serum albumin level was lower in the severe CKD group than in the other two groups.

Type of gastrectomy, surgical approach, and extent of LN dissection were similar in all three groups. The duration of the surgery, however, was significantly shorter for the severe and mild CKD groups than for the control group.

Short-term outcomes

Table 2 details the incidence of postoperative complications. A total of 236 complications were observed in 223 patients. The overall complication rates for the severe CKD, mild CKD, and control groups were 36.7, 28.1, and 21.2 %, respectively. The incidence of complications was associated with CKD staging. The severe and mild CKD groups were more likely to manifest anastomotic leakage and intraabdominal abscess than the control group, whereas wound infection and pulmonary and cardiovascular complications were significantly more frequent in the severe

Table 1 Patient characteristics

Characteristic	Severe CKD ($n = 49$)	Mild CKD ($n = 128$)	Control ($n = 798$)	p
Sex				0.186
Male	33 (67.3 %)	101 (79.0 %)	575 (72.1 %)	
Female	16 (32.7 %)	27 (21.0 %)	223 (27.9 %)	
Age	70.5 ± 7.4	71.6 ± 8.3	63.9 ± 11.3	<0.001[a]
Co-morbidity other than CKD				<0.001
No	24 (48.9 %)	53 (41.4 %)	504 (63.2 %)	
Yes	25 (51.1 %)	75 (58.6 %)	294 (36.8 %)	
Depth of invasion				0.296
pT1a	11 (22.4 %)	34 (26.6 %)	224 (28.1 %)	
pT1b	13 (26.5 %)	36 (28.1 %)	220 (27.6 %)	
pT2	12 (24.5 %)	12 (9.4 %)	105 (13.2 %)	
pT3	8 (16.3 %)	30 (23.4 %)	136 (17.0 %)	
pT4a	5 (10.2 %)	16 (12.5 %)	103 (12.9 %)	
pT4b	0 (0 %)	0 (0 %)	10 (1.3 %)	
Lymph node metastasis				0.318
pN0	30 (61.2 %)	79 (61.7 %)	534 (66.9 %)	
pN1	8 (16.3 %)	15 (11.7 %)	96 (12.0 %)	
pN2	6 (12.2 %)	19 (14.8 %)	67 (8.4 %)	
pN3a	3 (6.1 %)	13 (10.2 %)	68 (8.5 %)	
pN3b	2 (4.1 %)	2 (1.6 %)	33 (4.1 %)	
Stage				0.262
pIA	19 (38.8 %)	56 (43.8 %)	394 (49.4 %)	
pIB	9 (18.4 %)	14 (10.9 %)	101 (12.7 %)	
pIIA	6 (12.2 %)	23 (18.0 %)	79 (9.9 %)	
pIIB	6 (12.2 %)	7 (5.5 %)	61 (7.6 %)	
pIIIA	5 (10.2 %)	9 (7.0 %)	46 (5.8 %)	
pIIIB	1 (2.0 %)	8 (6.3 %)	50 (6.3 %)	
pIIIC	1 (2.0 %)	6 (4.7 %)	45 (5.6 %)	
pIV	2 (4.1 %)	5 (4.0 %)	22 (2.8 %)	
Hb (g/dl)	10.4 ± 1.8	12.6 ± 1.9	13.3 ± 2.0	<0.001[b]
Alb (g/dl)	3.8 ± 0.6	4.2 ± 0.4	4.3 ± 0.4	<0.001[c]
Cr (mg/dl)	4.5 ± 3.3	1.1 ± 0.2	0.7 ± 0.1	<0.001[d]
GFR (ml/min/1.73 m^2)	16.6 ± 10.5	50.6 ± 6.6	80.7 ± 15.6	<0.001[d]
CEA (ng/ml)	11.1 ± 38.7	5.1 ± 7.3	7.3 ± 38.0	0.392
Gastrectomy				0.164
Distal, PPG	38 (77.6 %)	82 (64.1 %)	513 (64.3 %)	
Total, proximal	11 (22.4 %)	46 (35.9 %)	285 (35.7 %)	
Approach				0.311
Open	42 (85.7 %)	106 (82.8 %)	629 (78.8 %)	
Laparoscopic	7 (14.3 %)	22 (17.2 %)	169 (21.2 %)	
Lymph node dissection				0.220
D1	34 (69.4 %)	86 (67.2 %)	498 (62.4 %)	
D2	15 (30.6 %)	42 (32.8 %)	300 (37.6 %)	
EBL (ml)	348 ± 270	436 ± 431	429 ± 439	0.438
Duration of operation (min)	258 ± 53	263 ± 91	284 ± 85	0.001[a]

Data are presented as mean ± SD or number (%)

CKD chronic kidney disease, *Hb* hemoglobin, *Alb* albumin, *Cr* creatinine, *GFR* glomerular filtration rate, *CEA* carcinoembryonic antigen, *PPG* pylorus-preserving gastrectomy, *EBL* estimated blood loss

[a] Significant difference between the severe CKD group and the control group and the mild CKD group and the control group; no difference between the severe CKD group and the mild CKD group (post-hoc multiple comparison using the Games–Howell procedure)

[b] Significant difference between the severe CKD group and the mild CKD group, the severe CKD group and the control group, and the mild CKD group and the control group (post-hoc multiple comparison using Tukey's procedure)

[c] Significant difference between the severe CKD group and the control group and the severe CKD group and the mild CKD group; no difference between the mild CKD group and the control group (post-hoc multiple comparison using the Games–Howell procedure)

[d] Significant difference between the severe CKD group and the mild CKD group, the severe CKD group and the control group, and the mild CKD group and the control group (post-hoc multiple comparison using the Games–Howell procedure)

CKD group than in the other two groups. Only one patient in the control group experienced acute renal failure, but he recovered renal function without dialysis. Serious postoperative complications—graded as IIIa or more according to the CD classification—were observed more frequently in the CKD groups than in the control group.

Table 2 Surgical complications

Parameter	Severe CKD ($n = 49$)	Mild CKD ($n = 128$)	Control ($n = 798$)	p
No. of patients with at least one complication	18 (36.7 %)	36 (28.1 %)	169 (21.2 %)	0.014
Local complication				
Anastomotic leakage	4 (8.2 %)	12 (9.4 %)	26 (3.3 %)	0.003
Pancreatic-related infection	4 (8.2 %)	6 (4.7 %)	35 (4.4 %)	0.473
Intraabdominal abscess	3 (6.1 %)	7 (5.5 %)	14 (1.8 %)	0.010
Wound infection	5 (10.2 %)	4 (3.1 %)	13 (1.6 %)	<0.001
Delayed gastric emptying	2 (4.1 %)	1 (0.8 %)	33 (4.1 %)	0.173
Ileus	0	0	13 (1.6 %)	0.232
Systemic complication				
Pulmonary	5 (10.2 %)	3 (2.3 %)	10 (1.3 %)	<0.001
Cardiovascular	3 (6.1 %)	2 (1.6 %)	3 (0.4 %)	<0.001
Acute renal failure	0	0	1 (0.1 %)	0.222
Other	2 (4.1%)	2 (2.3 %)	23 (2.9 %)	0.825
Postoperative hospital stay (days)	35.7 ± 37.5	35.6 ± 72.7	27.3 ± 24.6	0.145
In-hospital death	3 (6.1 %)	2 (2.3 %)	3 (0.4 %)	<0.001
Clavien–Dindo classification				0.017
Grade II	7 (38.9 %)	19 (52.8 %)	111 (65.7 %)	
Grade IIIa	6 (33.3 %)	11 (30.6 %)	37 (21.9 %)	
Grade IIIb	1 (5.6 %)	3 (8.3 %)	17 (10.1 %)	
Grade IVa	1 (5.6 %)	1 (2.8 %)	1 (0.6%)	
Grade V	3 (16.7 %)	2 (5.6 %)	3 (1.8%)	

Data are presented as the mean ± SD or the number (%)

The incidence of in-hospital mortality in the CKD groups was associated with CKD staging.

Table 3 shows the correlation between serious surgical complications and clinical findings in patients with mild and severe CKD. Patients who had co-morbidities other than CKD developed more severe complications than patients with only CKD. The serum albumin level was significantly lower in patients with severe complications than those without them. Also, estimated blood loss was seen significantly more often in patients with severe complications than in patients without complications. The duration of surgery was longer in patients with severe complications than in those without those complications. More patients who underwent total gastrectomy and D2 lymphadenectomy had severe complications than did those who underwent distal gastrectomy and D1 lymphadenectomy. However, the difference was not statistically significant.

We also compared the incidence of local and systemic complications between early (1997–2004) and late (2005–2011) periods in each group. There were no significant differences in the incidence of anastomotic leakage, intraabdominal abscess, wound infection, delayed gastric emptying, cardiovascular complications, or pulmonary complications between the two periods. Pancreatic-related infection, however, was observed more frequently during the late period than during the early period in the mild CKD group (8.0 vs. 0 %, $p = 0.035$) and the control group (6.6 vs. 1.9 %, $p = 0.011$).

Long-term outcomes

The median follow-up duration for all patients was 1,674 days. The OS rates for the severe CKD, mild CKD, and control groups were, at 3 years 48.6, 80.9, and 85.0 %, respectively, and at 5 years 28.6, 76.2, and 80.0 %, respectively. The log-rank test revealed a significant difference between the severe CKD group and the other two groups. However, there were no significant differences between the mild CKD and control group. In addition, the 3- and 5-year OS rates for patients with CKD stage 4 were 37.6 and 18.8 %, respectively, and those for patients with CKD stage 5 were 50.3 and 26.8 %, respectively, but the differences were not significant (data not shown). Furthermore, the 3- and 5-year OS rates for patients with maintenance hemodialysis in the severe CKD group were 49.5 and 18.6 %, respectively. There was no significant difference between patients with maintenance hemodialysis and other patients in the severe CKD group. During follow-up, maintenance dialysis was

Table 3 Correlation between surgical complications, which are categorized according to the Clavien–Dindo classification as IIIa or more, and clinical findings in patients with mild and severe CKD

Clinical finding	Complications ($n = 28$)	No complications ($n = 149$)	p
Sex			0.924
Male	21	113	
Female	7	36	
Age	70.7 ± 6.2	71.5 ± 8.3	0.620
Co-morbidity other than CKD			0.045
No	11	89	
Yes	17	60	
Hb (g/dl)	11.5 ± 2.0	12.2 ± 2.1	0.112
Alb (g/dl)	3.9 ± 0.6	4.2 ± 0.4	0.001
Cr (mg/dl)	2.4 ± 2.3	2.0 ± 2.3	0.406
GFR (ml/min/1.73 m^2)	38.1 ± 19.5	41.9 ± 16.8	0.281
CEA (ng/ml)	6.1 ± 8.1	6.9 ± 22.3	0.869
Gastrectomy			0.079
Distal, PPG	15	105	
Total, proximal	13	44	
Surgical approach			0.150
Open	26	122	
Laparoscopic	2	27	
Lymph node dissection			0.079
D1	15	105	
D2	13	44	
Estimated blood loss (ml)	802 ± 472	350 ± 350	<0.001
Duration of operation (min)	308 ± 74	256 ± 84	0.003

Data are presented as mean ± SD or as the number (%)

initiated for four patients (three from the severe CKD group, one from the mild CKD group) between 6 and 60 months following gastrectomy.

Table 4 lists the causes of death in all groups. Although 73.2 % of deaths in the control group were due to GC recurrence, more than 60 % patients in the severe CKD group died of causes other than GC. The number of patient deaths due to cardiovascular and cerebrovascular events, pneumonia, and infection increased as the extent of the CKD progressed.

Univariate analysis revealed that the following factors significantly affected the survival of patients undergoing GC in the severe and mild CKD groups after curative gastrectomy: co-morbidity other than CKD, hemoglobin (Hb) <12 g/dl, albumin (Alb) <3.5 g/dl, carcinoembryonic antigen (CEA) ≥5.0 ng/ml, severe CKD, tumor stage, estimated blood loss >400 ml, and the presence of surgical complications (Table 5). Multivariate analysis revealed

Table 4 Causes of death

Cause of death	Severe CKD ($n = 24$)	Mild CKD ($n = 32$)	Control ($n = 157$)
Gastric cancer	5 (20.8 %)	19 (59.4 %)	115 (73.2 %)
Other cancer	1 (4.1 %)	1 (3.1 %)	15 (9.6 %)
Other disease	15 (62.5 %)	10 (31.3 %)	24 (15.3 %)
Cardiovascular disease	4 (16.7 %)	3 (9.4 %)	6 (3.8 %)
Cerebrovascular disease	3 (12.5 %)	1 (3.1 %)	1 (0.6 %)
Pulmonary disease	3 (12.5 %)	4 (12.5 %)	4 (2.5 %)
Infection	4 (16.7 %)	1 (3.1 %)	4 (2.5 %)
Other	1 (4.1 %)	1 (3.1 %)	9 (5.7 %)
In-hospital death	3 (12.5 %)	2 (6.3 %)	3 (1.9 %)

Data are presented as number (%)

that Alb <3.5 g/dl, severe CKD, tumor stage, and the presence of surgical complications were independent prognostic factors.

Discussion

Improved medical care has increased the longevity of patients with CKD, resulting in more surgeries. However, few data has been reported regarding gastrectomy in patients with CKD. To our knowledge, the current study is the first to compare short- and long-term surgical outcomes after gastrectomy according to distinct CKD stages. Interestingly, the severity of CKD was associated with an incremental increase in surgical complications, a higher surgical mortality rate, and a diminished OS rate.

Local and systemic postoperative complications were more common in the CKD groups than in the control group. Specifically, the rate of anastomotic leakage in the severe and mild CKD groups was more than twofold greater than that in the control group. Furthermore, several studies reported that renal dysfunction increased the risk of anastomotic leakage following gastrointestinal surgery [12–14]. Recently, we reported that CKD is an independent risk factor for esophagojejunal anastomotic leakage [15]. In the present study, all incidences of anastomotic leakage in the control group occurred at esophagojejunal anastomoses. In contrast, in the severe and mild CKD groups, 5 of 16 (31 %) leakages were in patients with gastroduodenostomy involving Billroth I reconstruction and 1 of 16 (6 %) occurred in the duodenal stump of a distal gastrectomy. Anastomotic leakage is rare when distal gastrectomy is performed in patients with normal renal function. However, surgeons should pay considerable attention to

Table 5 Univariate and multivariate analyses of prognostic factors for GC in patients with CKD

Factor	Overall survival					
	Univariate analysis			Multivariate analysis		
	p	HR	95 % CI	*p*	HR	95 % CI
Age	0.287	1.019	0.984–1.055	0.297	1.021	0.982–1.061
Sex (male vs. female)	0.402	0.779	0.435–1.397			
Co-morbidity other than CKD (yes vs. no)	0.038	1.760	1.033–3.003	0.218	1.449	0.803–2.618
Hb (<12 vs. ≥12 g/dl)	< 0.001	2.915	1.675–5.051	0.321	1.403	0.719–2.732
Alb (<3.5 vs. ≥3.5 mg/dl)	< 0.001	5.000	2.571–9.709	0.012	2.874	1.266–6.536
CEA (≥5.0 vs. <5.0 ng/ml)	0.004	2.203	1.288–3.767	0.196	1.479	0.817–2.677
CKD (severe vs. mild)	<0.001	3.266	1.885–5.660	0.035	2.252	1.060–4.784
Stage (II, III, IV vs. I)	<0.001	2.959	1.709–5.102	<0.001	3.205	1.706–6.024
Lymphadenectomy extent (D1 vs. D2)	0.414	0.793	0.454–1.383			
EBL (≥400 vs. <400 ml)	0.015	1.936	1.140–3.288	0.207	1.451	0.814–2.587
Operation duration (≥260 vs. <260 min)	0.680	1.122	0.651–1.931			
Surgical complication (yes vs. no)	0.002	2.320	1.364–3.947	0.026	1.899	1.078–3.344

HR hazard ratio, *CI* confidence interval

esophagojejunal and gastroduodenal anastomoses when performing gastrectomy in patients with CKD.

In the CKD groups, other frequent local complications were intraabdominal abscess and wound infection. These results contradicted a previous study by Mori et al. [16], who reported no significant difference in the incidence of postoperative infection between patients with nonuremic renal failure and those with normal renal function. Nevertheless, the mean sCr level in our study patients with mild and severe CKD was 2.0 mg/dl, which were much worse than the 0.9 mg/dl reported by Mori et al. Furthermore, uremia is associated with alternations in primary host immune responses, which increases the risk of bacterial infection [17]. Moreover, immune response deficiency is common, and humoral immune defense is often compromised in patients with CKD. Thus, further research is warranted to clarify the mechanisms of infection susceptibility in patients with CKD following gastrectomy.

In the present study, cardiovascular and pulmonary complications were observed frequently during the perioperative period following gastrectomy. They were also determined to be significant causes of death in patients with CKD. This finding is in accordance with a study reporting the short-term surgical outcome that baseline CKD is a risk factor for cardiovascular complications after major surgery [18]. Go et al. [19] also reported that in patients with progressive CKD there was an independent graded association observed between reduced GFR and risk of death and cardiovascular events. Also, CKD was associated with pathophysiological changes in many systems, which ultimately induced cardiovascular events, such as accelerated atherosclerosis, hypertension, and metabolic acidosis. As expected, a markedly higher percentage of cardiovascular complications after gastrectomy were observed in the severe CKD group and was also one of the major causes of death of patients in that group. In addition, pulmonary complications after gastrectomy were more frequently observed in the severe CKD group. Gastrectomy itself poses a risk of aspiration pneumonia because gastroesophageal reflex is a common complication. Thus, patients with CKD are particularly considered at increased risk of pneumonia and pulmonary complications [20, 21].

The preoperative management of patients with CKD can be challenging. Several factors such as preoperative assessment, anemia, blood pressure control, cardiopulmonary function, and correction of a bleeding diathesis must be considered simultaneously to decrease surgery-related morbidity and mortality. Loss of erythropoietin secretion upon CKD progression is a major factor contributing to anemia. Therefore, therapy with iron supplementation and erythropoietin-stimulating agents currently targets patients with hemoglobin concentrations between 11 and 12 g/dl (hematocrit 33–36 %) [22]. Systemic hypertension is the most common cardiovascular complication in patients with CKD. Effective management of hypertension is dependent on restriction of sodium and fluid intake plus potent antihypertensive therapy [23]. The Kidney Disease Outcome Quality Initiative guideline recommends a blood pressure goal of <130 mmHg systolic and <80 mmHg diastolic for all patients with CKD, with rennin–angiotensin axis blockers as first-line antihypertensive drugs for renoprotection [24]. Welten et al. [25] reported that β-blocker therapy in patients with CKD who are undergoing major noncardiac vascular surgery reduced short- and long-term mortality. Pulmonary rehabilitation before upper abdominal surgery was reported to be effective for preventing

pulmonary complications [26]. There is a need to validate whether these protocols could reduce cardiovascular and pulmonary complications and improve prognosis after gastrectomy in patients with CKD. In addition, patients with severe CKD showed that uremic platelet dysfunction can be caused by perioperative bleeding. Dialysis, 8-deamino-D-arginine vasopressin (DDAVP) cryoprecipitate, or estrogens can improve platelet function in these patients [27]. Surgeons should also pay attention to operative blood loss and surgery duration for reducing postoperative complications.

The OS rate for patients with an estimated GFR of <30 ml/min/1.73 m^2 was associated with a strikingly poor prognosis after gastrectomy. In this study, the 5-year OS rate of this group was 28.6 %, which was much worse than that of a recent report of surgical outcomes of colorectal cancer patients with CKD (75 % in the CKD stage 5 group) [28]. Although an explanation for this discrepancy is not clear, we speculate that the nutritional status of patients who underwent gastrectomy was worse than that of those who underwent colorectal resection because gastrectomy may be associated with nutrition-related complications such as dumping syndrome, postvagotomy diarrhea, fat maldigestion, and nutrient deficiencies. Furthermore, malnutrition and inflammation are common and often concurrent, and hypoalbuminemia was independently associated with high mortality in patients with CKD [29–31]. Hypoalbuminemia is a prognostic factor in patients with CKD and those with GC [32]. In accordance with these previous studies, we confirmed hypoalbuminemia as an independent prognostic factor for patients with CKD following gastrectomy. Also, hypoalbuminemia was associated with severe surgical complications. Thus, a future prospective study is warranted to evaluate whether correcting hypoalbuminemia through perioperative nutrition management can improve surgical outcomes of gastrectomy in patients with CKD.

Not only the short-term but also the long-term outcomes after gastrectomy for the patients with severe CKD were poor. A total of 15 patients with severe CKD after gastrectomy died of causes other than GC, and 9 of them died within 3 years of surgery. Furthermore, the risk of morbidity and in-hospital mortality in patients with severe CKD was higher than that of patients without severe CKD. Therefore, it may be worthwhile for surgeons to consider avoiding gastrectomy in patients with severe CKD who have early-stage GC.

There were some limitations in our study. First, we conducted a retrospective analysis, implying that there was an inherent selection bias regarding the surgical procedure, which might have affected the incidence of surgical complications. However, in the reports included in this study, the surgeons preferred a more simple procedure to treat early GC in the upper third of the stomach in patients with CKD, as Roux-en-Y reconstruction was selected more often than proximal gastrectomy followed by jejunal interposition. Nevertheless, anastomotic leakage or abdominal abscess was more frequent in the CKD groups than in the control group. Second, the mean patient ages among the three groups were different. Therefore, the prognoses for the patients with CKD may have been worse than for those in the control group. Even if the patients aged <60 years were omitted from the control group, the prognosis of the CKD group was still worse than that of the control group (data not shown). Third, there were a relatively small number of patients in the severe CKD group. Patients with CKD stage 4 or 5 were categorized in the same group (i.e., the severe CKD group) because their incidences of surgical complications were similar and their prognoses did not differ. Thus, a multicenter study with an increased number of patients with CKD would more effectively evaluate surgical outcomes following gastrectomy. Finally, the duration of this study was long. Hence, during this study period new surgical techniques, instruments, and perioperative management may have been developed. However, the surgical complication rates and long-term outcomes did not differ between the early and late periods of this study.

Conclusions

Despite of the efforts for intensive preoperative management, reducing the extent of surgery and operative blood loss, and shortening the duration of the surgery, both short- and long-term outcomes of gastrectomy in CKD patients with GFR <30 ml/min/1.73 m^2 were poor. Additional studies with large cohorts are essential to refine the risk stratification for gastrectomy in patients with CKD.

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