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Original Article

Safety and feasibility of laparoscopic surgery for elderly rectal cancer patients in Japan: a nationwide study

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Abstract

Background: This study aimed to analyse the perioperative results from a national dataset of rectal cancer resections in elderly patients.

Methods: The clinical records of patients undergoing rectal cancer surgery between 2012 and 2014 were retrieved from the Japanese National Clinical Database and analysed retrospectively. Patients were categorized according to age and those 80 years or older were defined as elderly. Subgroups were also defined according to the surgical approach (laparoscopy *versus* open surgery). The short-term outcomes, including mortality, anastomotic leak, surgical site infections and medical complications were compared between subgroups.

Results: Of 56 175 patients undergoing rectal cancer surgery, some 6717 patients were elderly and laparoscopy was performed in 46.8 per cent of the sample. When comparing laparoscopy and open surgery in elderly patients, the operative mortality rate (1.5 *versus* 2.8 per cent; $P < 0.001$), the incidence of anastomotic leakage (5.2 *versus* 6.5 per cent; $P = 0.026$), surgical site infections (6.0 versus 8.0 per cent; $P = 0.001$), pneumonia (1.4 versus 2.5 per cent; $P = 0.001$), renal failure (0.7 versus 1.3 per cent; $P = 0.016$) and cardiac events (0.3 *versus* 0.8 per cent; $P = 0.008$) were lower for laparoscopy than for open surgery. The overall complication rate in elderly patients (19.5 per cent) was comparable to that in the younger group ($P = 0.07$). However, incidence of systemic complications was significantly higher in elderly than in younger patients (all $P < 0.001$).

Conclusion: Laparoscopy was safe and feasible in elderly patients compared with open surgery. However, the rates of systemic complications were significantly higher than in younger patients.

Introduction

Accumulated worldwide evidence has shown that laparoscopic surgery for colorectal cancer provides a number of benefits to patients that lead to better and faster recovery[1–4]. Despite the widespread use of laparoscopy, its safety in elderly patients has not been fully evaluated.

Recent systematic reviews and meta-analyses have reported positive effects of laparoscopy on short-term outcomes for elderly patients [5–8]. As described elsewhere, the benefit from laparoscopy in elderly patients are faster bowel movement recovery, earlier discharge and fewer postoperative complications[9–12]. However, elderly patients are generally considered to have a higher risk of postoperative mortality and complications than non-elderly patients because they have an increased number of concomitant diseases or poorer performance status[13,14]; moreover, a laparoscopic approach requires a longer operation time in the Trendelenburg position using pneumoperitoneum[15]. Therefore, the selection of laparoscopy in elderly patients needs to be carefully considered, and whether or not all elderly patients benefit from laparoscopy is a matter of debate.

The present study aimed to assess the short-term outcomes of laparoscopy in elderly rectal cancer patients.

Methods

Data collection

All data were retrieved from the Japanese National Clinical Database (NCD). The details of data registration system in this database are described elsewhere[16]. Approximately 1 200 000 surgical cases are registered annually, which corresponds to more

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than 95 per cent of all surgeries in Japan. This nationwide project was started in 2011 and includes all cases registered since then. Although a few institutions missed the registration date in 2011 and registered later, currently more than 98 per cent of surgeries are included in the NCD[17]. The variable items in the NCD are based on the definitions of those of the American College of Surgeons' National Surgical Quality Improvement Program. Data of all patients who had undergone rectal surgeries for rectal cancer located lower than the sigmoid rectum between 2012 and 2014 were extracted. Any records that were not included by patients or were without information on patient age or sex were excluded from the analysis. The patients were classified into the following four age categories: less than 60 years, 60–69 years, 70–79 years and 80 years or over. The patient backgrounds (age, sex, presence of diabetes/chronic obstructive pulmonary disease (COPD), smoking/alcohol habits, co-morbidities, ASA physical status classification grade, history of presurgical chemotherapy or radiotherapy, and oncological findings) were extracted. Surgery-related factors (procedure, open surgery or laparoscopy, operation time, blood loss and stoma construction) were also extracted. The extracted variables were selected based on the previous study that had investigated postoperative complications in rectal surgery from NCD data[17].

Endpoints

The postoperative short-term outcomes of operative mortality and postoperative complications were the primary endpoints. Postoperative complications included anastomotic leakage (AL), surgical site infection (SSI), pneumonia, urinary tract infection (UTI), renal failure, central nervous system (CNS) complications and cardiac complications. AL and SSI were defined as surgery-related complications, whereas others were defined as systemic complications not related to surgery. Surgical factors, such as operating time and blood loss, were also included in the analysis as secondary outcomes.

Statistical analysis

The software package STATA®15 (STATA Corp., College Station, Texas, USA) was used for all statistical analyses. The χ^2 test was performed for all comparisons among multiple variables. Multivariate logistic regression analysis was performed on the variables associated with operative mortality, including laparoscopy, metastasis (M1b cases), gender (male), daily activities with any assistance, congestive heart failure, peritoneal metastases, weight loss greater than 10 per cent, systemic sepsis, ASA 3 or lower, haemoglobin less than 13.5 g/dl (male) or less than 12.5 g/dl (female), platelets less than $8 \times 10^4/\mu l$, albumin less than 3.5 g/dl, aspartate aminotransferase (AST) greater than 40 U/l, urea nitrogen greater than 25 mg/dl, sodium less than 135 mmol/l, prothrombin time–international normalized ratio (PT-INR) greater than 1.1, white blood cell count (WBC) greater than 9000/μl. Statistical significance was set at $P < 0.05$. All graphs were generated by using GraphPad Prism®8 (GraphPad Software, San Diego, California, USA).

Results

Study population

Some 56 175 patients who underwent surgical resection for rectal cancer during the study period were selected and categorized into four age groups. *Table 1* shows the clinical features of patients in each age category, reporting a significant difference in sex distribution (61.8 per cent were males less than 60 years old and 54.6 per cent were males at least 80 years old, $P < 0.001$). The smoking and alcohol habit rates were higher in the youngest age category (less than 60 years old) than in the others (smoking habit, 28.0 per cent, and alcohol habit, 30.5 per cent, in the less than 60-year-old group; both $P < 0.001$). As expected, the rates of co-morbidities, including COPD and pneumonia, were highest in the 80 years and older cohort (COPD, 5.5 per cent and pneumonia, 0.6 per cent in the 80 years and older category; both $P < 0.001$).

On the other hand, the 70–79-year-old cohort had the highest rate of diabetes among all categories (21.0 per cent, $P < 0.001$). The rate of high ASA grade (grade 3 and above) was greatest in the 80 years and older cohort (18.7 per cent, $P < 0.001$). In respect of the oncological features, the 80 years and older cohort reported a prevalence of progressive tumours (14.3 per cent for T4a or worse, $P < 0.001$) but less nodal or distant metastases (37.8 per cent for N1a and 7.4 per cent for M1a or worse, both $P < 0.001$). Preoperative chemotherapy and radiotherapy were the most frequently performed treatments in the youngest age category (chemotherapy, 3.2 per cent, and radiotherapy, 3.7 per cent, in the less than 60 years category; both $P < 0.001$).

Additionally, the operation time was longer in the youngest age group (291 minutes in the less than 60 years cohort and 243 minutes in the 80 years and older cohort, $P < 0.001$) and blood loss was higher in the youngest age category (288 ml in the less than 60 years cohort and 237 ml in the 80 years and older cohort, $P < 0.001$).

Short-term outcomes in the elderly patients

The postoperative short-term outcomes were compared between open surgery and laparoscopy in the 80 years and older cohort. As shown in *Fig. 1*, both operative mortality and overall postoperative complication rates were significantly lower for laparoscopy than for open surgery (open surgery 2.8 per cent *versus* laparoscopy 1.5 per cent, $P < 0.001$ for operative mortality; open surgery 21.1 per cent *versus* laparoscopy 17.7 per cent, $P < 0.001$ for overall complications). AL and SSI were both significantly reduced in laparoscopy for 80 years and older patients (open surgery 6.5 per cent *versus* laparoscopy 5.2 per cent, $P = 0.026$ for AL; open surgery 8.0 per cent *versus* laparoscopy 6.0 per cent, $P = 0.001$ for SSI) (*Fig. 2*). Of note, the overall AL rate in this study was 8.8 per cent. The incidences of all of systemic complications (postoperative pneumonia, UTI, renal failure, CNS complications and cardiac events) in the 80 years and older patients were significantly lower for laparoscopy than for open surgery (open surgery 2.5 per cent *versus* laparoscopy 1.4 per cent, $P = 0.001$ for pneumonia; open surgery 1.9 per cent *versus* laparoscopy 1.1 per cent, $P = 0.006$ for UTI; open surgery 1.3 per cent *versus* laparoscopy 0.7 per cent, $P = 0.016$ for renal failure; open surgery 1.1 per cent *versus* laparoscopy 0.5 per cent, $P = 0.010$ for CNS complications; and open surgery 0.8 per cent *versus* laparoscopy 0.3 per cent, $P = 0.009$ for cardiac complications).

Short-term outcomes among all age categories

The short-term outcomes in open surgery and laparoscopy were also analysed in the younger age categories, and then compared with those of the 80 years and older cohort. As shown in *Fig. 2*, all of the major outcomes after laparoscopy were significantly improved in the other age categories, although the operative mortality rate was higher in the 80 years and older cohort (*Fig. 1*). The trends in systemic complications were different between the less than 60 years cohort and the 80 years and older cohort following open surgery and laparoscopy. The incidences of pneumonia, renal failure, CNS complications and cardiac complications were

Table 1 Clinical features

	<60 years ($n = 13\,313$)	60–69 years ($n = 19\,108$)	70–79 years ($n = 17\,037$)	≥80 years ($n = 6717$)	*P*
Gender (male)	8232 (61.8)	13 212 (69.1)	11 136 (65.4)	3669 (54.6)	<0.001
Diabetes	1352 (10.2)	3467 (18.1)	3535 (21.7)	1148 (17.1)	<0.001
Smoking habit	3734 (28.0)	4873 (25.5)	2706 (15.9)	585 (8.7)	<0.001
Alcohol habit	4056 (30.5)	6121 (32.0)	4125 (24.2)	916 (13.6)	<0.001
COPD	125 (0.9)	523 (2.7)	707 (4.1)	371 (5.5)	<0.001
ASA ≥3	478 (3.6)	1290 (6.8)	1808 (10.6)	1255 (18.7)	<0.001
≥T4a	1826 (13.7)	2683 (14.0)	2156 (12.7)	961 (14.3)	<0.001
≥N1a	5410 (40.6)	7595 (39.7)	6486 (38.1)	2536 (37.8)	<0.001
≥M1a	1258 (9.4)	1833 (9.6)	1360 (8.0)	499 (7.4)	<0.001
PreCT	423 (3.2)	465 (2.4)	315 (1.8)	44 (0.7)	<0.001
PreRT	498 (3.7)	536 (2.8)	312 (1.8)	45 (0.7)	<0.001

Values in parentheses are percentages. COPD, chronic obstructive pulmonary disease; PreCT, preoperative chemotherapy; PreRT, preoperative radiotherapy.

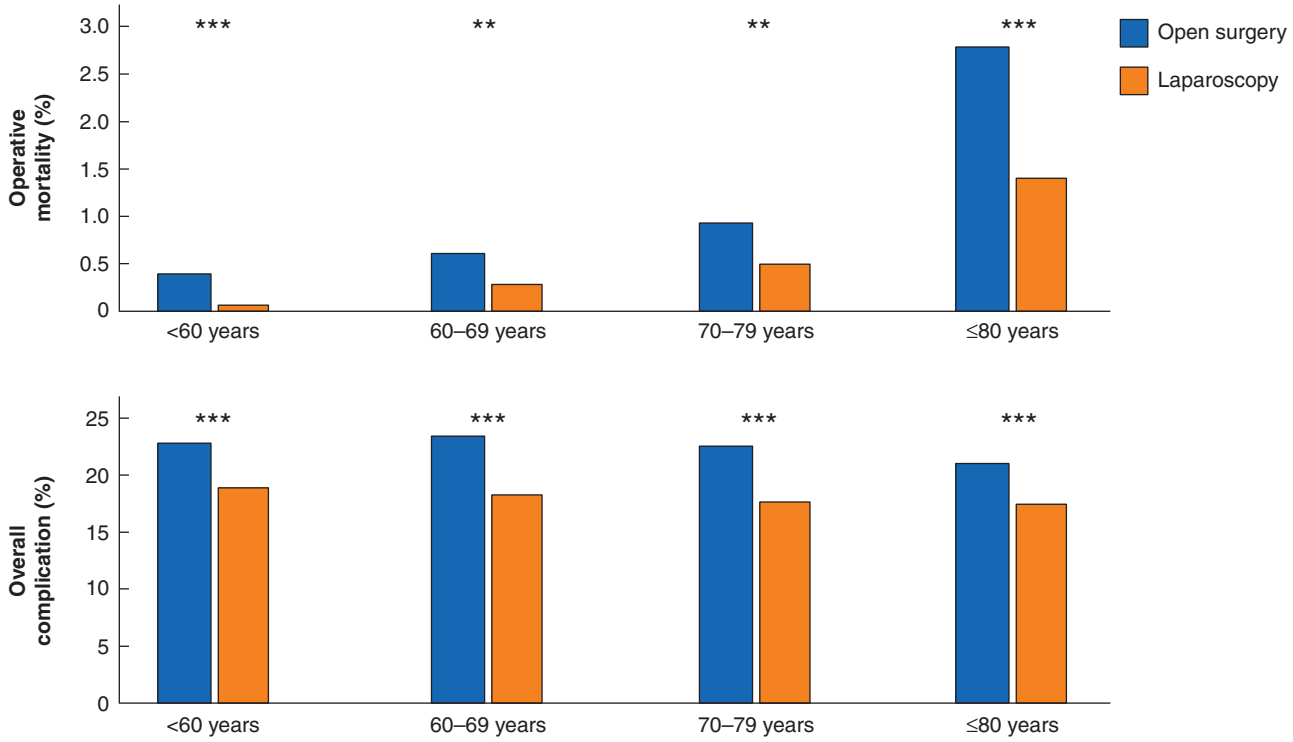

Fig. 1 Comparison of operative mortality and overall postoperative complications between open surgery and laparoscopy in each age category

*** $P < 0.001$, ** $P < 0.01$.

similar in the less than 60 years cohort (open surgery 0.4 per cent *versus* laparoscopy 0.3 per cent, $P = 0.166$ for pneumonia; open surgery 0.6 per cent *versus* laparoscopy 0.5 per cent, $P = 0.105$ for renal failure; open surgery 0.3 per cent *versus* laparoscopy 0.5 per cent, $P = 0.195$ for CNS complications; and open surgery 0.1 per cent *versus* laparoscopy 0.1 per cent, $P = 0.876$ for cardiac complications).

Table 2 shows various postoperative short-term outcomes in each age category, including both laparoscopy and open surgery. Operative mortality was significantly higher in the 80 years and older cohort (2.2 per cent, $P < 0.001$), but there was no significant difference in the overall postoperative complication rate (19.5 per cent, $P = 0.07$) among all age categories. Interestingly, both the AL and SSI rates were significantly lower in the elderly patients (5.9 per cent for AL and 7.0 per cent for SSI, both $P < 0.001$). Note that the stoma construction rate in the 80 years and older cohort was 8.9 per cent, which was lower than that in the younger age cohort (10.8 per cent in the less than 60 years cohort). More importantly, systemic complications, such as pneumonia (2.0 per cent, $P < 0.001$), renal failure (1.0 per cent, $P = 0.001$), UTI (1.5 per cent, $P = 0.001$), CNS complications (0.8 per cent, $P < 0.001$) and cardiac complications (0.5 per cent, $P < 0.001$) were all significantly more frequently observed in the 80 years and older cohort than in the younger cohort.

Multivariate analysis for the risk of operative mortality in elderly patients

Table 3 shows the results of multivariate analysis for the risk of operative mortality in the 80 years and older cohort. M1b cases (hazard ratio (HR) 2.82, 95 per cent c.i. 1.24 to 6.41), male (HR 2.51, 95 per cent c.i. 1.67 to 6.41), activities of daily livings with any assistance (HR = 2.80, 95 per cent c.i. 1.92 to 4.10), presence of congestive heart failure (HR = 2.94, 95 per cent c.i. 1.46 to 5.93), systemic sepsis (HR = 5.44, 95 per cent c.i. 2.13 to 13.87),

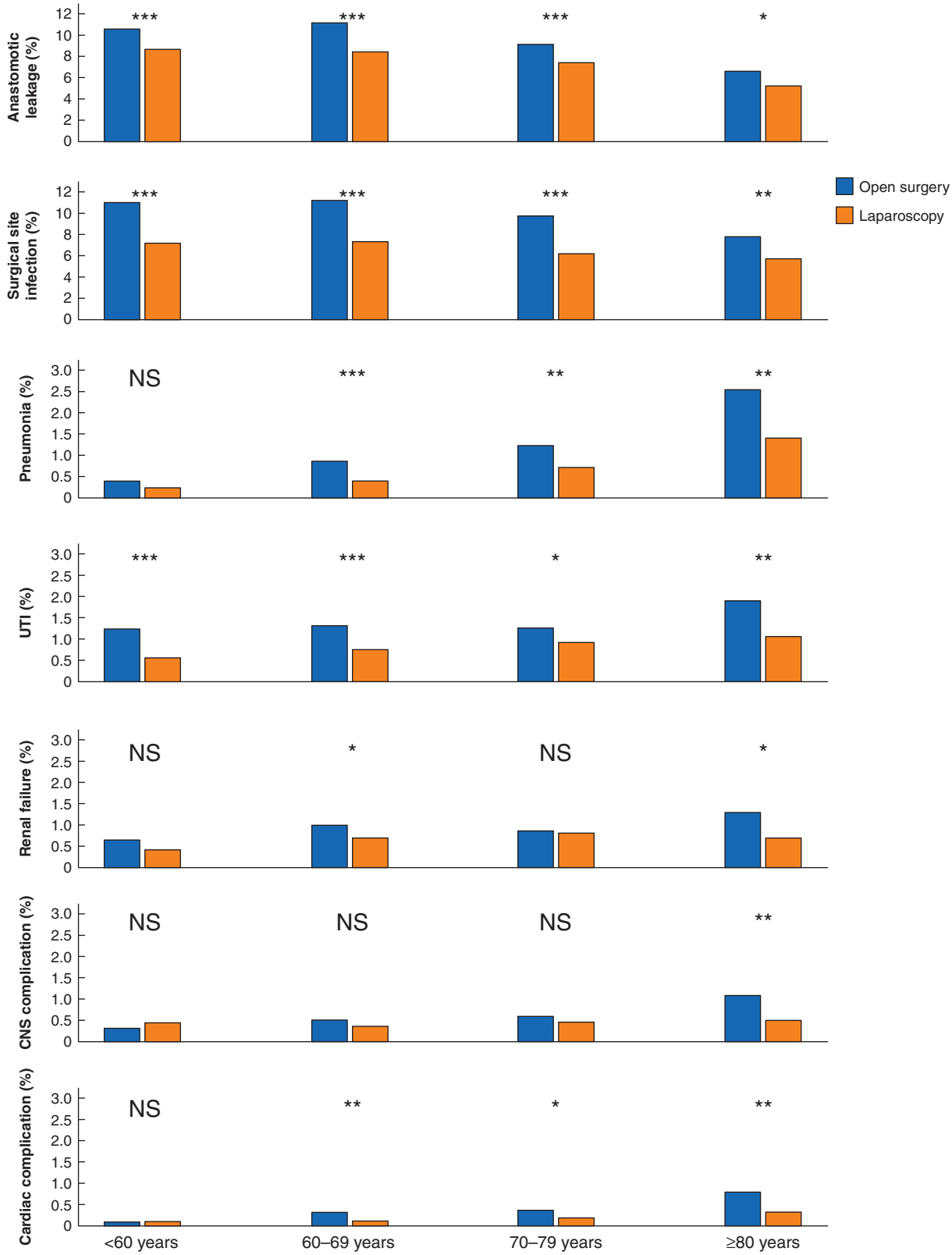

Fig. 2 Comparison of surgery-related and systemic complications between open surgery and laparoscopy in each age category

UTI, urinary tract infection; NS, not significant; *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$.

low haemoglobin (HR = 1.81, 95 per cent c.i. 1.14 to 2.89), low platelets (HR = 3.97, 95 per cent c.i. 1.32 to 11.96), high AST (HR = 2.17, 95 per cent c.i. 1.28 to 3.69), low sodium (HR = 1.72, 95 per cent c.i. 1.04 to 2.86), extended PT–INR (HR = 1.71, 95 per cent c.i. 1.13 to 2.57) and high WBC (HR = 2.08, 95 per cent c.i. 1.28 to 3.37) were all statistically significant risk factors. More

Table 2 Comparison of postoperative short-term outcomes in each age category

Outcome	<60 years ($n = 13\,313$)	60–69 years ($n = 19\,108$)	70–79 years ($n = 17\,037$)	≥80 years ($n = 6717$)	*P*
Operative mortality	29 (0.2)	86 (0.5)	117 (0.7)	146 (2.2)	<0.001
Overall complication	2755 (20.7)	3967 (20.8)	3411 (20.0)	1310 (19.5)	0.07
AL	1272 (9.6)	1864 (9.8)	1403 (8.2)	394 (5.9)	<0.001
SSI	1178 (8.8)	1761 (9.2)	1370 (8.0)	473 (7.0)	<0.001
Pneumonia	44 (0.3)	118 (0.6)	166 (1.0)	136 (2.0)	<0.001
UTI	115 (0.9)	189 (1.0)	187 (1.1)	102 (1.5)	<0.001
Renal failure	72 (0.5)	163 (0.9)	147 (0.9)	68 (1.0)	<0.001
CNS complication	54 (0.4)	85 (0.4)	93 (0.5)	57 (0.8)	<0.001
Cardiac complication	15 (0.1)	38 (0.2)	45 (0.3)	36 (0.5)	<0.001

Values in parentheses are percentages. SSI, surgical site infection; AL, anastomotic leakage; UTI, urinary tract infection; CNS, central nervous system.

Table 3 Multivariate analysis of risk factors for operative mortality in the 80 years and older cohort ($n = 6717$)

Risk factor	HR (95% c.i.)	*P*
Laparoscopic surgery	0.68 (0.47–0.99)	0.043
M1b cases	2.82 (1.24–6.41)	0.013
Gender (male)	2.51 (1.67–6.41)	<0.001
ADL with any assistance	2.80 (1.92–4.10)	<0.001
Congestive heart failure	2.94 (1.46–5.93)	0.003
Peritoneal metastases	1.38 (0.66–2.89)	0.399
Weight loss >10%	1.53 (0.83–2.82)	0.170
Systemic sepsis	5.44 (2.13–13.87)	<0.001
ASA ≤3	1.35 (0.92–1.97)	0.124
Haemoglobin <13.5 g/dl (male) <12.5 g/dl (female)	1.81 (1.14–2.89)	0.013
Platelets <8 × 10^4/μl	3.97 (1.32–11.96)	0.014
Albumin <3.5 g/dl	1.41 (0.96–2.07)	0.080
AST >40 U/l	2.17 (1.28–3.69)	0.004
Urea nitrogen >25 mg/dl	1.49 (0.96–2.32)	0.074
Sodium <135 mmol/l	1.72 (1.04–2.86)	0.036
PT-INR >1.1	1.71 (1.13–2.57)	0.011
WBC >9000/μl	2.08 (1.28–3.37)	0.003

HR, hazard ratio; ADL, activities of daily living; AST, asparate aminotransferase; PT-INR, prothrombin time–international normalized ratio; WBC, white blood cell count.

importantly, laparoscopy was a significant factor for reducing the operative mortality rate (HR = 0.68, 95 per cent c.i. 0.47 to 0.99).

Discussion

Despite recent improvements in surgical techniques and perioperative care in colorectal surgery, the higher mortality rate in elderly patients is still an issue. In fact, the mortality rate in colorectal surgery has been recently reported to range from 2.8 to 7 per cent[18,19]. A meta-analysis of 30 studies comparing open surgery and laparoscopy showed significant reduction in not only postoperative complications but also perioperative mortality in laparoscopy for elderly patients[7], consistent with the present findings.

Especially in elderly patients, complications such as AL or SSI can lead to significant loss of quality of life and sometimes be associated with mortality[20]. Even in recent investigations, the AL rate has been reported as ranging between 0.78 and 15.9 per cent for left-sided anastomosis[21–28]. Of note, in the present series, the incidence of AL and SSI were significantly reduced in laparoscopy groups both in the 80 years and older cohort and the younger cohorts. Surprisingly, however, the AL and SSI incidence in the 80 years and older cohort were significantly lower than those in the younger age categories despite their lower stoma construction rate.

Unlike surgery-related complications, there was a major difference in trends in systemic complications, such as cardiopulmonary, renal or CNS complications. All such complications were significantly reduced in laparoscopy only in the 80 years and older cohort but not in the younger cohorts. Given that almost half of the 80 years and older patients underwent laparoscopy, this result provides supportive evidence that laparoscopy is more beneficial for elderly patients than younger patients, as reported previously[29]. In some recent studies, aged or frail patients were reported to benefit from laparoscopy more than younger patients[30,31]. Although the definitive reason has not been elucidated yet, the present data also showed a similar trend.

The elderly patients tended to have higher incidences of systemic complications but not of surgery-related complications. These results imply that the higher operative mortality rate in the elderly patients could have been because of the higher incidence rate of systemic complications rather than because of AL or SSI. To reduce such postoperative systemic complications, perioperative management, such as prehabilitation or enhanced recovery pathways, are becoming more important[32]. A network meta-analysis including 40 studies has shown that enhanced recovery protocols significantly reduce postoperative complications in both open surgery and laparoscopy[33]. The protocols have a series of evidence-based care elements to support recovery by reducing body stress from surgery[34]. Such stress reduction is particularly important for elderly patients who often have co-morbidities and are considered to be a high-risk population. However, the effects of such perioperative management protocols were not evaluated in the present study; this could be considered in future investigations.

There are several limitations in this study. First is the lack of long-term outcome evaluation. However, long-term outcomes of very old patients might be difficult to evaluate, due to their generally shorter life expectancy. Second, there is a possible selection bias due to the retrospective nature of the study, which could have had an impact on the decision to treat patients with laparoscopy. The third limitation is that there was no information regarding the severity of each complication so a detailed risk analysis could not be performed.

Improvement in the perioperative care of elderly patients to reduce systemic complications should be a continuing goal.

Disclosure. The authors declare no conflict of interest.

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