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Laparoscopy-assisted gastrectomy in the elderly: experience from a UK centre

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ABSTRACT
BACKGROUND   Gastric cancer has a high incidence in the elderly in the UK, with a significant number of patients aged 75 years or more. While surgery forms the mainstay of treatment, evidence pertaining to the management of gastric cancer in the Western population in this age group is scarce.
METHODS   We retrospectively reviewed the outcomes of laparoscopy-assisted total and distal gastrectomies at our centre from 2005 to 2015. Patients aged 70 years or above were included in the elderly group.
RESULTS   A total of 60 patients underwent laparoscopy-assisted gastrectomy over a 10-year period, with a predominance of male patients. There was no significant difference in the rate of overall surgical and non-surgical complications, in-hospital mortality, operation time and length of hospital stay, between the elderly and non-elderly groups. Univariate analysis, performed for risk factors relating to anastomotic leak and surgical complications, showed that age over 70 years and higher American Association of Anesthesiologists grades are associated with a higher, though not statistically significant, number of anastomotic leaks ($P = 1.000$ and $P = 0.442$, respectively) and surgical complications ($P = 0.469$ and $P = 0.162$, respectively). The recurrence rate within the first 3 years of surgery was significantly higher in the non-elderly group compared with the elderly group (Log Rank test, $P = 0.002$). There was no significant difference in survival between the two groups (Log Rank test, $P = 0.619$).
CONCLUSIONS   Laparoscopy-assisted gastrectomy is safe and feasible in an elderly population. There is a need for well-designed, prospective, randomised studies with quality of life data to inform our practice in future.

Introduction

Gastric cancer is the fifth most common cancer and the third most common cause of cancer-related deaths worldwide.[1] In the UK, it is the 16th most common cancer, with a male predominance, and accounts for 2% of all new cases of cancer diagnosed.[2] There has been a decreasing trend in the incidence of gastric cancer recently, which may be attributed to a decrease in the incidence of *Helicobacter pylori* and lifestyle changes.[3–5] The laparoscopic approach to the treatment of gastric cancer, in the form of a laparoscopy-assisted distal gastrectomy, was first described by Kitano *et al.* in 1994.[6] Laparoscopic total gastrectomy with lymph node dissection, which was first reported by Uyama *et al.* in 1999,[7] while being technically more demanding, is being increasingly used to treat gastric cancer.[8,9] A number of studies have shown laparoscopic distal and total gastrectomy to be safe in the elderly.[10,11] However, the evidence pertaining to the management of gastric cancer in this age group in the Western population is relatively sparse.[12,13] We retrospectively reviewed the outcomes of laparoscopy-assisted total and distal gastrectomies at our centre, with a view to assessing the potential benefits of this approach in the UK population.

Methods

Data collection

A retrospective review of a prospectively maintained database of laparoscopic distal and total gastrectomy for adenocarcinoma undertaken from 2005 to 2015 at University

Hospital Aintree was performed. The Hospital Episode Statistics data were inspected for any missing patients from our database. The study was approved by the hospital's research and development department. Written, informed consent was obtained from all the patients.

Data including patient demographics, American Society of Anesthesiologists (ASA) physical status grade, preoperative diagnosis and perioperative outcomes, including operating time, type of resection, intra- and postoperative complications, hospital stay and 30-day mortality, were collected. Oncological outcomes, including resection margins, lymph node status, stage of tumour, recurrence and survival, were noted. Patients 70 years and above were included in the elderly group.

Operative technique

All cases had a preoperative histological diagnosis of gastric adenocarcinoma on endoscopy and were discussed at the hospital multidisciplinary team meeting prior to surgery. All patients underwent a staging laparoscopy prior to definitive surgery, in keeping with the British Society of Gastroenterology guidelines for the management of gastric cancers.[14] Laparoscopic gastrectomy, together with either D1 or D2 lymph node dissection was performed. Port positions routinely used in the procedure are shown in Fig 1. Roux-en-Y oesophagojejunal, retrocolic end to side anastomosis was performed laparoscopically using a stapling gun (Covidien EEA™, Minneapolis, MN), in the case of total gastrectomy. The rigid anvil was broken by removing the spring to convert it into a flip-top and was passed orally using a nasogastric tube (as in the later Orvil™ by Covidien) that was pulled out through a hole made in the cross-stapled oesophagus. The Orvil™ was trialled in three cases but there were technical issues relating to its use (the anvil edge popped out,

with a possibility of perforating the oesophagus) and hence its use was discontinued.

In patients undergoing distal gastrectomy, a Billroth II retrocolic side-to-side (Roux-en-Y) gastrojejunostomy was performed with a laparoscopic linear stapler. Enterotomies were closed by intracorporeal stitches and the staple line was reinforced with intracorporeal nonabsorbable sutures. A retrieval bag was used to extract the specimen, through a 5-cm utility incision, by extending the left sided 12-mm port site. The same incision was used to perform an extracorporeal jejuno-jejunal side-to-side anastomosis using a linear stapling device.

Postoperative care

Patients were admitted to the high dependency unit for 24–48 hours after resection. Oral water-soluble contrast swallow was performed on the fourth day following total gastrectomy and the next day following distal gastrectomy. Patients were started on oral liquids if the contrast swallow did not show an anastomotic leak. Patients were reviewed routinely by a physiotherapist and a dietician during the postoperative period.

Follow-up

Patients were followed up at two weeks in clinic, following discharge from hospital. Subsequent follow-ups were arranged at three-monthly intervals in the first year, six-monthly intervals in the second year and on an annual basis thereafter. There was a very low threshold for investigating patients with cross-sectional imaging and endoscopy where there were any symptoms suspicious of recurrence identified in the history and clinical examination during follow up. All patients were followed up for five years after surgery for gastric cancer.

Statistical methods

Data were analysed using the SPSS statistical software program (SPSS Inc., Chicago, IL). The unpaired t-test was used to compare quantitative variables if they were normally distributed and the Mann-Whitney U test was used when the distribution of variables was skewed. Patient demographics and operative characteristics were compared using the Fisher's exact test or the Chi-square test. Survival and recurrence were calculated using the Kaplan–Meier method and compared using the log-rank (Mantel-Cox) test. A P value less than 0.005 was considered to be statistically significant.

Results

A total of 60 patients underwent laparoscopy-assisted gastrectomy over a 10-year period (2005–2015) at a university hospital in the UK. Of these, 39 were male and 21 were female, with a mean age of 71.71 years (range 44–90 years); 39 patients (65%) were 70 years or above and 16 (26.7%) were 80 years or above. Patient characteristics are summarised in Table 1. Patients 70 years or older were grouped as elderly and those of less than 70 years were grouped as non-elderly in our study. Both groups were comparable in most characteristics. There were more patients with high-grade
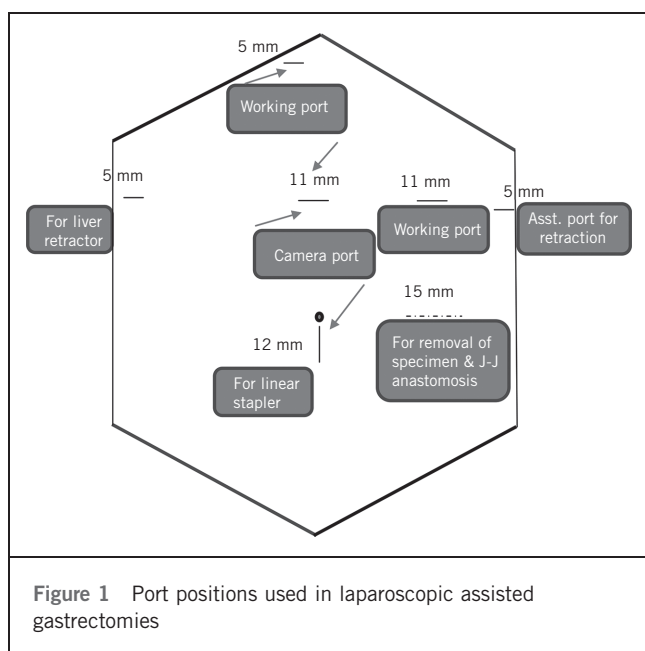

Figure 1 Port positions used in laparoscopic assisted gastrectomies

Table 1 Characteristics of 60 patients who underwent laparoscopy-assisted gastrectomy between 2005 and 2015 at Aintree University Hospital, UK

Characteristic	Elderly		Non-elderly	P value[a]
	Age ≥ 70 (*n* = 39)	Age ≥ 80 (*n* = 16)	Age < 70 (*n* = 21)	
Age in years (SD)	78.5 (4.9)	83.25 (3.2)	59.1 (8.1)	< 0.0001[b]
Sex:				0.088[c]
Male *n* (%)	22 (56.4)	8 (50)	17 (80.9)	
Female *n* (%)	17 (43.6)	8 (50)	4 (19.0)	
ASA grade:				0.063[c]
3, 4 *n* (%)	25 (64.1)	10 (62.5)	8 (38.1)	
1, 2 *n* (%)	14 (35.9)	6 (37.5)	13 (61.9)	
Body mass index	25.9 (4.7)	25.8 (4.9)	26 (4.7)	0.938[d]
Histology:				0.009[e]
Well differentiated *n* (%)	8 (20.5)	1 (6.3)	9 (42.9)	
Moderately differentiated *n* (%)	16 (41)	77 (43.7)	1 (4.8)	
Poorly differentiated *n* (%)	15 (38.5)	8 (50)	11 (52.4)	
TNM stage:				0.930[e]
High-grade dysplasia	1 (2.6)	0	1 (4.8)	
I	22 (56.4)	9 (56.2)	11 (52.4)	
II	12 (30.8)	5 (31.3)	7 (33.3)	
III	3 (7.7)	2 (12.5)	2 (9.5)	
IV	1 ((2.6)	0	0	

ASA, American Association of Anesthesiologists; SD, standard deviation; [a]P value represents comparison between elderly and non-elderly age group; [b] Mann-Whitney U test; [c] Fisher's exact test; [d] Unpaired t-test; [e] Chi-square test

tumours in the elderly group as compared with the non-elderly group. Age and histology were significantly different between elderly and non-elderly groups ($P < 0.05$). A majority (62.5%) of patients in the 80 years or above age group were ASA grade 3 or 4 . All patients in this age group underwent D2 gastrectomy. None of these patients developed chest infection, one patient had an anastomotic leak, one patient had a duodenal stump leak, and there was one mortality following a myocardial infarction.

There was no significant difference between the two groups with respect to the type of gastrectomy, mean operation time and intraoperative complications (Table 2). However, there was a significantly higher number of D2 lymph node dissections performed in the elderly group as compared with the non-elderly group (38 vs 16, $P = 0.017$). Median lymph node harvest for the non-elderly group was 27 (range 4–96) and for the elderly group was 25.5 (range 4–74). Median lymph node harvest for D1 gastrectomy cases was 29 (5–60) and for D2 gastrectomy cases was 25.5 (4–96).

There were no conversions to an open procedure. The resection margin was positive in one patient in whom a metastatic nodule from the peritoneum was also excised. Frozen sections for both specimens, performed intraoperatively, did not show any evidence of neoplasia.

There was no significant difference in the rate of overall surgical and non-surgical complications between the two groups (Table 3). There was no significant difference in the rate of anastomotic leak and duodenal stump leak in the two groups. Of the seven patients with anastomotic leaks, three had to return to theatre for a laparotomy, one patient was managed conservatively, one had an abdominal drain that had perforated through the anastomosis, which settled when the drain was withdrawn, and two had radiological guided drainage of the leaks, which settled with time.

There was no significant difference in the hospital mortality rate between the two groups (Table 3). There were three mortalities in the elderly group: one patient had a massive haemorrhage postoperatively from coeliac axis. This patient also had an anastomotic leak. Another patient died after suffering two consecutive myocardial infarctions within a two-week interval. The third patient died from respiratory failure following a severe chest infection and was diagnosed with a late anastomotic leak, 22 days after surgery. This patient also had a bile duct injury during surgery, which was managed with t-tube drainage. A water-soluble oral contrast swallow on the fifth day postoperatively did not detect a leak. Subsequent computed tomography with oral contrast did not show contrast leak or any significant intraabdominal collection.

Table 2 Operative outcomes for 60 patients who underwent laparoscopy-assisted gastrectomy between 2005 and 2015 at Aintree University Hospital, UK

Operative outcome	Elderly		Non-elderly	P value[a]
	Age ≥ 70 (*n* = 39)	Age ≥ 80 (*n* = 16)	Age < 70 (*n* = 21)	
Gastrectomy:				0.287[b]
Distal *n* (%)	21 (53.8)	9 (56.3)	8 (38.1)	
Total *n* (%)	18 (46.2)	7 (43.6)	13 (61.9)	
Lymph node dissection:				0.017[b]
D1 (%)	1 (2.6)	0	5 (23.8)	
D2 (%)	38 (97.4)	16 (100)	16 (76.2)	
Median operating time in minutes (range)	510.5 (339–815)	510 (339–670)	510 (382–690)	0.092[c]
Complications:				0.537[b]
Small bowel injury	1 (2.6)	1 (6.3)	0	
Common bile duct injury	1 (2.6)	0	0	

[a] Comparison between elderly and non-elderly age group; [b] Fisher exact test; [c] Mann-Whitney U test

Table 3 Postoperative outcomes for 60 patients who underwent laparoscopy-assisted gastrectomy between 2005 and 2015 at Aintree University Hospital, UK

Postoperative outcome	Elderly		Non-elderly	P value[a]
	Age ≥ 70 (*n* = 39)	Age ≥ 80 (*n* = 16)	Age < 70 (*n* = 21)	
Surgical complications *n* (%)	8 (20.5)	3 (18.8)	2 (4.8)	0.469[b]
Anastomotic leak *n* (%)	5 (12.8)	1 (6.3)	2 (4.8)	1.000[b]
Duodenal stump leak *n* (%)	1 (2.6)	1 (6.3)	0	1.000[b]
Nonsurgical complications:	4 (10.2)	1 (6.3)	2 (9.5)	1.000[b]
Chest infection *n* (%)	1 (2.6)	0	2 (9.5)	
Cardiac *n* (%)	2 (5.1)	1 (6.3)	0	
Acute pancreatitis *n* (%)	1 (2.6)	0	0	
Median hospital stay in days (range)	9 (6–95)	9 (6–72)	8 (5–99)	0.0784[c]
In-hospital mortality *n* (< 30 days)	3 (7.7)	1 (6.3)	0	0.545[b]

[a] Comparison between elderly and non-elderly age group; [b] Fisher exact test; [c] Mann-Whitney U test

The leak was identified using oral methylene blue, which was seen leaking in the abdominal drain. There was no significant difference in the rate of non-surgical complications between the two groups (Table 3).

In total, 10 patients had recurrence of cancer. All recurrences occurred within the first three years following surgery. There were eight recurrences in the non-elderly group as compared with two in elderly group (Fig 2, log rank test *P* = 0.002). Patients were followed up at our centre every three months in the first year following gastrectomy, every six months in the second year and once a year subsequently. There was a very low threshold for investigating patients with cross-sectional imaging and endoscopy where were any symptoms suspicious of recurrence identified in the history and clinical examination during follow-up. However, it is challenging to ascertain the cause of death of patients who have died in the community, with no hospital admission in the follow-up period. There were no recurrences identified in the elderly age group other than the two patients identified within the first three years. There was no significant difference in survival between the two groups (Fig 3, log rank test, *P* = 0.619).

Univariate analysis was performed for risk factors relating to anastomotic leaks specifically and overall surgical (intra-
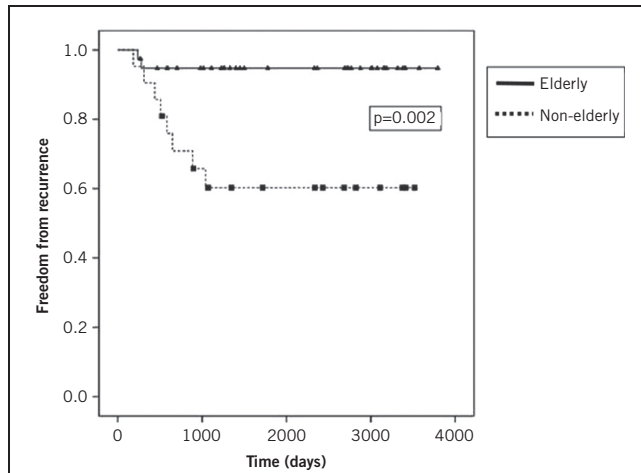
Figure 2 Kaplan–Meir chart comparing recurrence in the elderly (age ≥ 70) and non-elderly (age < 70) groups
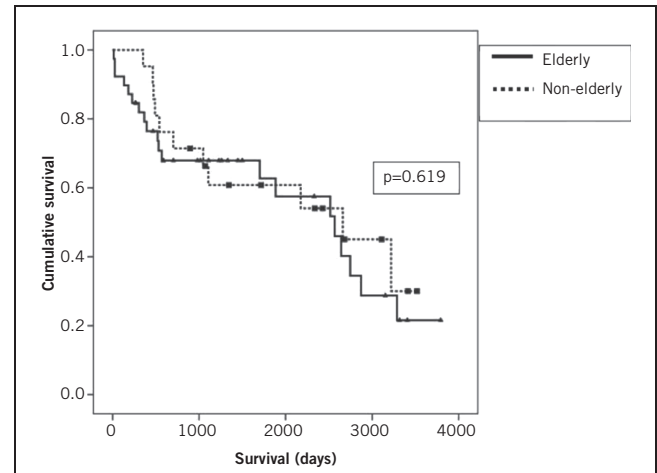

Figure 3 Kaplan–Meir chart comparing survival in the elderly (age ≥ 70) and non-elderly (age < 70) groups

and postoperative) complications (Tables 4 and 5). Patients in the elderly group and those with higher ASA grades had a higher number of anastomotic leaks and surgical complications but this difference was not statistically significant. While all anastomotic leaks and surgical complications occurred following D2 resections, there was no significant difference when compared with D1 resections ($P = 1.000$).

Six patients in each group received neoadjuvant chemotherapy but none of these 12 patients completed adjuvant chemotherapy because they were not considered to be fit enough for this after surgery.

Discussion

Life expectancy continues to rise in the UK.[15] Age is associated with a decrease in functional reserve, making elderly individuals less able to withstand the trauma and stress of surgery, which may result in a higher rate of complications and mortality.[16] Age greater than 70 years has been shown to be an independent predictor of increased postoperative complications, in-hospital mortality and longer hospital stay.[17] More than half the number of patients diagnosed with gastric cancer in 2011–2013 in the UK were aged 75 years or more.[2] Surgical resection continues to form the mainstay of treatment for patients with gastric cancer. However, there is a dearth of evidence relating to the management of gastric cancer in the elderly in the Western population.[12,15] In this study, we have shown that laparoscopy-assisted gastrectomy in the elderly population, which was defined as 70 years and above, is feasible and safe, with outcomes that are comparable to those in a non-elderly population.

Laparoscopic distal gastrectomy has been shown to be a safe procedure, associated with a shorter hospital stay and fewer complications as compared with open surgery.[18,19] Laparoscopic total gastrectomy, while being technically more demanding, has also been described to be safe and effective in experienced hands, with fewer postoperative

complications and a shorter hospital stay as compared with open surgery.[20] Laparoscopic gastrectomy thus offers potential benefits that would be particularly relevant in elderly patients.

The patient selection and the choice of the operation, in our study, were made through the local multidisciplinary team in keeping with nationally recommended guidelines.[14] However, data about the decision to palliate surgically or endoscopically were not available. While it has been shown that the more extensive the surgery for gastric cancer and lymph nodal dissection, the higher is the morbidity,[21] our study has shown that there is no significant added risk in performing curative D2 resections in the elderly, which is in keeping with existing studies.[10–12,22,23] Recent evidence supports a modified D2 resection, sparing the spleen and pancreatic lymph nodes in the elderly and might expand its suitability in this group of patients.[24] In our study, a significantly higher number of D2 resections were performed in the elderly group of patients. There was no significant difference in the rate of complications and mortality between the two groups in our study. Age greater than 65 years, male sex and the extent of nodal dissection were reported by the Dutch Gastric Cancer Trial to be important risk factors for mortality.[25] The recurrence rate was significantly lower in the elderly as compared with the non-elderly in this study, which might be due to the fact that the number of D2 resections was significantly higher in this group. There was no significant difference in survival between the two groups, which is in keeping with a number of studies.[22,26] Coniglio et al.found that cancer stage correlated with survival in the elderly (≥ 80 years) and non-elderly (< 80 years) populations,[26] which is similar to the findings of Pisanu et al.[12] The study by Endo et al.showed that sex, the extent of gastric resection, the extent of lymph node dissection and blood loss were significant prognostic factors for overall survival.[27]

Table 4 Univariate analysis of risk factors for anastomotic leak in 60 patients who underwent laparoscopy-assisted gastrectomy between 2005 and 2015 at Aintree University Hospital, UK

Risk factor	Anastomotic leak		P value
	Yes (n = 7)	No (n = 53)	
Age (years):			1.000[a]
≥70 n (%)	5 (71.4)	34 (64.2)	
< 70 n (%)	2 (28.6)	19 (35.8)	
Sex:			0.687[a]
Male n (%)	4 (57.1)	35 (66)	
Female n (%)	3 (42.9)	18 (34)	
ASA grade:			0.442[a]
3, 4 n (%)	5 (71.4)	28 (52.8)	
1, 2 n (%)	2 (28.6)	25 (47.2)	
Histology:			0.448[b]
Well differentiated n (%)	1 (14.3)	16 (30.2)	
Moderately differentiated n (%)	2 (28.6)	15 (28.3)	
Poorly differentiated n (%)	3 (42.9)	23 (43.4)	
TNM staging:			0.282[b]
High-grade dysplasia	0	2 (3.8)	
I	4 (57.1)	29 (54.7)	
II	1 (14.3)	18 (33.9)	
III	2 (28.6)	3 (5.7)	
IV	0	1 (1.9)	
Type of gastrectomy:			0.426[a]
Distal n (%)	2 (28.6)	27 (50.9)	
Total n (%)	5 (71.4)	26 (49.1)	
Lymph node dissection:			1.000[a]
D1	0	6 (11.3)	
D2	7 (100)	47 (88.7)	
Operation time:			0.221[a]
< 360 minutes (%)	1 (14.3)	1 (1.9)	
> 360 minutes (%)	6 (85.7)	52 (98.1)	

[a] Fisher exact test; [b] Chi-square test

Table 5 Univariate analysis of risk factors for surgical complications in 60 patients who underwent laparoscopy-assisted gastrectomy between 2005 and 2015 at Aintree University Hospital, UK

Risk factor	Surgical complications		P value
	Yes (n = 10)	No (n = 50)	
Age (years):			0.469[a]
≥70 n (%)	8 (80)	31 (62)	
< 70 n (%)	2 (20)	19 (28)	
Sex:			0.729[a]
Male n (%)	6 (60)	33 (66)	
Female n (%)	4 (40)	17 (34)	
ASA grade:			0.162[a]
3, 4 n (%)	8 (80)	25 (50)	
1, 2 n (%)	2 (20)	25 (50)	
Histology:			0.179[b]
Well differentiated n (%)	1 (10)	16 (32)	
Moderately differentiated n (%)	5 (50)	12 (24)	
Poorly differentiated n (%)	4 (40)	22 (44)	
TNM staging:			0.536[b]
High-grade dysplasia	0	2 (4)	
I	6 (60)	27 (54)	
II	2 (20)	17 (34)	
III	2 (20)	3 (6)	
IV	0	1 (2)	
Type of gastrectomy:			0.732[a]
Distal n (%)	4 (40)	25 (50)	
Total n (%)	6 (60)	25 (50)	
Lymph node dissection:			0.577[a]
D1	0	6 (12)	
D2	10 (100)	44 (88)	
Operation time:			0.308[a]
< 360 minutes (%)	1 (10)	1 (2)	
> 360 minutes (%)	9 (90)	49 (98)	

[a] Fisher exact test; [b] Chi-square test

In our study, there was no significant association between age, sex, ASA grade, histological grade of tumour, tumour stage, type of gastrectomy, type of lymph node dissection and operation time and anastomotic leak or overall surgical complications. Higher Charlson comorbidity index (CCI) score (≥ 5) has been shown to be associated with a higher postoperative morbidity and in-hospital mortality in the elderly, defined as being 80 years or above, in a study by Hsu et al.[28] In a study by Fujisaki et al., CCI of ≥ 3, ASA grade and intraoperative blood loss of ≥ 50 ml were found to be

independent risk factors for postoperative complications on multivariate analysis.[29] However, age was not found to significantly affect the risk of postoperative complications in this study investigating laparoscopic gastrectomy in the elderly (≥ 75 years).[29] In a study by Yamada et al., wherein the elderly group was defined as being 85 years and above, ASA grade, CCI, forced expiratory volume at 1 second (FEV1) and serum albumin concentration correlated with the occurrence of postoperative pneumonia.[30] Tran et al. reported

that age (≥ 80 years defined as elderly), blood transfusion, serum albumin and creatinine were independent predictors of 90-day mortality rate and tumour stage. Tumour grade, race, blood transfusion and adjuvant therapy were independently associated with disease-specific survival.[13]

This study has some limitations. It was conducted retrospectively and had a relatively small sample size. It also lacked postoperative quality of life data reporting, which is seen as an accurate marker of patient-centred care and which would be particularly useful information in an elderly population.[31]

Conclusions

Laparoscopy-assisted gastrectomy for gastric cancer is safe and feasible in the elderly in the UK, with results comparable with the non-elderly population. There is a need for prospective, well-designed randomised studies, with quality of life data to better inform future practice.

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