NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of laparoscopic gastrectomy for cancer

Cancer of the stomach can be treated by partial or total removal of the stomach (gastrectomy) to take out the tumour and any affected lymph nodes. Gastrectomy was traditionally carried out by open surgery. In this procedure, the gastrectomy is performed using keyhole surgery. The cancer is then removed in exactly the same way as open surgery.

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in January 2008.

Procedure name

• Laparoscopic gastrectomy for cancer

Specialty societies

- Association of Laparoscopic Surgeons of Great Britain and Ireland
- Association of Upper Gastrointestinal Surgeons
- British Society of Gastroenterology

Description

Indications

Gastric cancer. Over 95% of gastric cancer is adenocarcinoma forming in the glandular cells of the stomach lining. Other types of gastric cancer include leiomyosarcoma, lymphoma, and carcinoid tumours.

Certain conditions, such as pernicious anemia, atrophic gastritis, Helicobacter pylori infection, or Barrett's oesophagus at the gastro-oesophageal junction may predispose to stomach cancer. Symptoms may include heartburn, dysphagia, bloating, loss of appetite, and weight loss. Nausea and vomiting may also occur and stools may contain blood. Further complications may include anemia.

Current treatment and alternatives

If patients present at a disease stage that is amenable to surgical treatment, the surgical treatment options for gastric cancer include laparoscopic gastric resection, or open gastrectomy.

What the procedure involves

The procedure is usually performed with a curative intent. Under general anaesthesia, a laparoscope and trocars are inserted through small incisions in the abdominal wall. A mini-laparotomy may be made for laparoscopically assisted gastrectomy. Surgery may involve total gastrectomy, or partial gastrectomy (either proximal or distal), the choice of total or partial gastrectomy is largely dependent on the site of the tumour. Some lymph nodes are usually dissected and removed, and an anastomosis is created (where the tumour has been removed) using a variety of techniques.

Efficacy

Survival: A multicentre case series (n = 1294 patients treated by laparoscopic surgery) reported 5 year disease free survival to be 99.8% for stage IA disease, 98.7% for stage IB disease, and 85.7% for stage II disease⁴. In a second case series in patients with more advanced disease 5-year overall and disease-free survival was 59% and 57% respectively, with overall survival ranging from 100% in stage 1A to 9% in stage IV³. The mortality rate due to cancer recurrence among patients undergoing laparoscopically assisted distal gastrectomy (LADG) was 5% (2/44) in one non randomised controlled trial¹. In a second non-randomised controlled trial 4% (1/24) of patients undergoing either partial or total laparoscopic gastrectomy died of metastatic cancer at 1 year follow up².

Lymph node dissection: Lymph node dissection is an important conceptual surrogate for curative resection completeness. In a meta analysis a significantly fewer number of lymph nodes were dissected with LADG than

ODG. Weighted mean difference -4.35 nodes (95% CI -5.73 to -2.98 nodes) (p<0.001) 5 .

Conversion to open surgery: Conversion from laparoscopic to open surgery was reported in between 2% $(1/44)^1$ of patients among the laparoscopic group in a non randomised controlled trial and in 1% $(14/1294)^4$ and 3% $(3/100)^3$ of patients in two case series. The reasons for conversion varied, but included anatomical constraints, bleeding, and mechanical problems.

Length of stay: Patients undergoing LADG were reported to have a hospital length of stay shortened by 5.5 days compared to those undergoing open gastrectomy in a meta analysis (p<0.001)⁵. In a case series of 111 patients undergoing a range of laparoscopic gastrectomy surgery the mean length of stay was 14.6 days⁶.

Blood loss: A meta analysis reported that there was significantly lower blood loss during LADG than with open gastrectomy, with a weighted mean difference of 146 ml (p<0.001)⁵.

Operative time: Operative time was reported to be significantly longer with LADG than with open gastrectomy in a meta analysis, with the weighted mean difference in time being 54.3 minutes (p<0.001)⁵. Conversely in one non randomised controlled trial the open procedure was 55 minutes shorter than LADG (p=0.006)¹.

Safety

A meta analysis of 1161 patients (837 treated by laparoscopic procedures) reported that there were fewer overall complications following LADG 11% (58/535) than following open gastrectomy 18% (97/519), odds ratio 0.54 $(p<0.001)^5$. However, specifically there was no significant difference between the groups with respect to mortality rate, anastomotic leak, anastomotic stricture, or wound infection.

There were significantly fewer cases of ileus following LADG than following open gastrectomy in a meta analysis, odds ratio $0.27 (p<0.02)^5$. In one multi centre case series of 1294 patients, ileus following laparoscopic gastric resection occurred in <1% (3/1294) of patients⁴.

One multicentre case series reported perforation (not otherwise described) in <1% (1/1294) of patients⁴. One non-randomised controlled trial of 102 patients (44 undergoing laparoscopic procedures) reported that there were more cases of pulmonary infection following open gastrectomy 10% (6/58) than following LADG 2% (1/44) for stomach cancer, however this difference was not statistically significant (p=0.110)¹.

Delayed gastric emptying requiring parenteral nutrition for 16 days occurred in 6% (1/16) of patients undergoing laparoscopic partial gastrectomy in one non-randomised controlled trial².

The rate of postoperative bleeding was reported as <1% (1/586)⁸, 1% (14/1294)⁴, and 2% (1/44)¹ across the included studies.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to laparoscopic gastrectomy for cancer. Searches were conducted via the following databases, covering the period from their commencement to 8 January 2008: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See appendix C for details of search strategy.)

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies.
	Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study.
	Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with gastric cancer requiring resection.
Intervention/test	Laparoscopic gastrectomy for cancer.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

Table 1 Inc	clusion criteria	for identification	of relevant studies
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List of studies included in the overview

This overview is based on one meta analysis⁵, two non randomised controlled trials^{1,2}, four case series^{3,6,4,8}, and one multiple case report⁷.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Existing reviews on this procedure

There were no published reviews identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B details the recommendations made in each piece of guidance listed below.

Interventional procedures

None

Technology appraisals

• Imatinib for gastrointestinal stromal tumours. NICE technology appraisal guidance 86 (2004). Available from www.nice.org.uk/TA086

Clinical guidelines

 Improving outcomes in colorectal cancer. NICE cancer service guideline (2004). Available from www.nice.org.uk/CSGCC

Public health guidance

• None

Table 2 Summary of key efficacy and safety findings on laparoscopic gastrectomy for cancer

Study details	Key efficacy findings	Key safety findings	Comments
Hosono S (2006)⁵ Meta analysis International, studies from Korea, Italy, and Japan	Clinical outcomes Time to passage of first flatus was achieved significantly earlier with LADG than ODG Weighted mean difference -0.68 days (95% CI -0.85 to -0.50) (p<0.001)	Postoperative complications Overall there were significantly fewer complications with LADG (58/535) than ODG (97/519), OR 0.54 (95% CI 0.37 to 0.77) (p<0.001).	No details provided of quality assessment of included studies, or whether this was taken into account in the analysis.
n=1611 (837 Laparascopic) 4 RCTs 12 NRCT's	There was a great deal of variability between studies in the length of stay. Overall length of stay was significantly shorted with LADG than ODG. Weighted mean difference -5.5 days (955	No significant difference in the rate of mortality between LADG 2% (2/101) and ODG 3% (3/105) (p=0.67) (Follow up period not stated.	Meta analysis presented both combined and separately for RCT and NRCT data.
Study aim: to elucidate the current status of LADG with regard to short term outcomes compared to ODG	CI -7.61 to -3.42) (p<0.001) Operative characteristics A significantly longer operative time was required with LADG than ODG. Weighted mean	No significant difference in the number of anastomotic leaks between LADG <1% (2/385) and ODG 3% (10/365) (p=0.10).	Searches limited to Embase Medline and Cochrane register, for publication between Jan 1991 and Aug 2006.
Study period: Various Population: Various	difference 54.3 minutes (95% CI 38.8 to 69.8 minutes) (p<0.001)	There was no significant difference in the incidence of anastomotic stenosis between LADG 3% (6/172) and ODG 3% (5/163)	Independent clinical appraisa and data extraction by two reviewers.
Indication: Early gastric cancer (definitions varied). Technique: Laparoscopically assisted distal gastrectomy.	Significantly less blood loss occurred with LADG than ODG. Weighted mean difference -145.6 ml (95% CI -181.4 to -109.9 ml) (p<0.001) A significantly fewer number of Lymph nodes were dissected with LADG than ODG. Weighted	(p=0.86). There were significantly fewer cases of ileus following LADG 1% (2/267) than ODG 5% (13/264), OR 0.27 (95% CI 0.09 to 0.84) (p<0.02)	Random effects model used f meta analysis. Test for heterogeneity undertaken.
Versus open distal gastrectomy. Versus open distal gastrectomy. Degree of lymph node excision varied between studies	mean difference -4.35 nodes (95% CI -5.73 to - 2.98 nodes) (p<0.001)	There was no significant difference in the incidence of wound infection between LADG 2% (9/448) and ODG 3% (13/421) (p=0.37).	No details provided of assessment of potential publication bias.
Follow up: not stated (to discharge)			

Study details	Key efficacy find	Key safety findin	gs			Comments			
Ziqiang W (2006) ¹	Clinical outcome	S			Complications				Concurrent but not deliberately
					Outcome	LADG	Open	p =	paired group of patients
Non-randomised controlled	5% (2/44) of patien during the 14-mon				Operative death	0%	4% (2/58)	NR	undergoing open surgery.
trial	patient (with stage recurrence, and al	IV cancer)	had port si	ite	Wound infection	2% (1/44)	4% (2/58)	NR	No details of independent outcome assessment
	months; another p				Anastomotic leak	0%	0%	NR	
China	metastases and ile 5% (3/58) of the o	pen surgery	group die	d during	Epididymitis	2% (1/44)	0%	NR	No significant difference in baseline demographic
n = 102 (44 Iaparoscopic)	follow-up, 2 of mul 1 of abdominal me	tastases of			Pulmonary infection	2% (1/44)	10% (6/58)	0.11	⁰ characteristics or TNM staging between the groups.
Study period:	Times to death no	t stated.			Gastrasthenia	2% (1/44)	4% (2/58)	NR	
March 2004–May 2005	Outcome Time to first flatus	LADG 4.1 ± (0.8)	Open 5.3 ±	p = 0.0	Cerebral infarction	2% (1/44)	2% (1/58)	NR	A mixed cohort of patients in terms of cancer stage at
Study aim: To investigate feasibility, safety and cancer	(days)	4.1 ± (0.0)	(1.0)	24	Anastomotic site bleeding	2% (1/44)	2% (1/58)	NR	baseline with patients from TNM IA to IV.
clearance of LADG with D2 lymphadenectomy.	Time to ground activities (days)	3.2 ± (0.8)	5.2 ± (1.3)	0.0 06					
Population: Age = 53 years (mean) Male = 58%.	Operative charac	teristics							
Indication: Malignant tumours on biopsy, in lower or middle part of the stomach. Patients with invasion of gastric serosa >10 cm ²	Conversion to ope (1/44) of patients I was encircled by e	because the	left gastric	c artery					
were excluded.	Outcome	LADG	Open	p =					
Technique: Laparoscopically	Operative time (min)	282.8 ± (32.8)	227.1 ± (21.9)	0.0 06					
assisted distal gastrectomy with D2 lymph node dissection under general anesthetic with 5-port	Intraoperative blood loss (ml)	139.3 ± (82.7)	331.4 ± (206.4)	0.0 11					
access, and 4 to 7 cm superior abdominal incision versus open	Proximal tumour margin (cm)	6.1 ± (1.3)	6.1 ± (1.0)	0.1 66					
distal gastrectomy. Follow up: mean 14 months	Distal tumour margin (cm)	6.4 ± (1.1)	6.0 ± (1.0)	0.1 78					
	Number of lymph nodes retrieved	30.1 ± (17.0)	33.2 ± (19.2)	0.7 98					
Conflict of interest: Not stated									
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Study details	Key efficacy f	indings				Key safety findings	Comments		
Dulucq J-L (2005) ²	Clinical outco	mes				Complications	Prospective study		
For "European data" it would be better to include, Huscher and also probably Azagra 2006 and Ibanez 2006 Non-randomised controlled	In the laparoso had died of me remaining patie port site metas groups 29% (8 disease) died o	tastatic c ents were tases. In /28) of pa	ancer at disease the oper atients (w	1 year, t -free with gastrec rith adva	he n no tomy	There was 1 incident of splenectomy during laparascopic surgery (4%; 1/24), compared with 5 incidences (18%; 5/28) during open surgery.	Patients with serosal invasion by the tumour on explorative laparoscopy were treated by open surgery.		
France	remaining patie recurrences at Outcome	ents were laparoto Lap	e disease my incisio Open	-free with on site. Lap.	Open	High fever, right abdominal pain and leukocytosis at 10-day follow-up occurred in 6% (1/16) of patients undergoing laparoscopic partial gastrectomy.	Unclear whether laparoscopic procedures were totally laparoscopic, or		
n = 52 (24 Iaparoscopic)	Ambulation (days)	total 3.1 ± (0.3)	total 6.2 ± (0.7)^	partial 2.5 ± (1.2)	partial 5.8 ± (1.0)^	Laparoscopic evaluation revealed an abscess and small duodenal fistula. Peritoneal lavage and drain placement	laparoscopically assisted.		
Study period: April 1995–March 2004	Time to first flatus (days) Length of stay (days)	3.6 ± (1.2) 16.9 ± (3.0)	4.7 ± (1.2)^ 24.0 ± (9.0)	2.9 ± (1.5) 16.0 ± (5.4)	5.8 ± (1.0)^ 25.0 ± (10.0)	resolved this. Delayed gastric emptying occurred in 6%	There were no significant differences in patient demographic characteristics at baseline. No details of cancer		
Study aim: To compare clinical outcomes and margin size between laparascopic and	^ p<0.05 vs eq	uivalent l	aparósco	. ,	. ,	(1/16) of patients undergoing laparoscopic partial gastrectomy, requiring parenteral nutrition for 16 days.	Stage at baseline reported.		
open gastrectomies Population: Mean age = 71 years. Male = 42%.	Operative cha Conversion to of patients afte laparoscopical	open sur r the dec	gery was		l in 0%	There were complications in 18% (5/28) of patients in the open surgery group, including 2 abscesses, 2 cases of delayed	gastric cancer (T3 and/or N1 or higher) received adjuvant chemo-radiotherapy.		
Indication: Malignant disease	Outcome	Lap total (n=8)	Open total (n=11)	Lap partial (n=16)	Open partial (n=17)	gastric emptying, and 1 death at 10 days from a cardiac event.	Different follow-up periods for the two groups makes		
diagnosed by endoscopy, unltrasonography, and dynamic CT scanning.	ASA* physical status score Operative time	1.7 ± (0.5) 183 ±	1.6 ± (0.4) 165 ±	1.7 ± (0.8) 130 ±	1.5 ± (0.5) 124 ±		comparison of disease-free survival difficult.		
Technique: Laparoscopic partial or total gastrectomy with 5-port access, and CO ₂ insufflation to 12 mmHG	(min) Intraoperative blood loss (ml) +ve margins Number of	(48) 81 ± (107) 0 24 ±	(60) 125 ± (95)^ 0 20 ±	(31) 60 ± (90) 0 17 ±	(22) 55 ± (50) 1 15 ±		Within the 24 patients treated by laparoscopic surgery, 19 had an adenocarcinoma, 2 had malignant stromal tumours, and 1 had a neuroendocrine		
versus partial or total open gastrectomy.	lymph nodes retrieved *American Soc	(12)	(8)	(7)	(4)		tumour Authors state that further		
Follow up: mean 29 months (lap), 34 months (open)	^ p<0.05 Vs ec	luivalent	laparosco	opic proc	edure		randomised studies are required to enforce their results		
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Conflict of interest: Not stated									

Study details	Key efficacy findings	Key safety findings		Comments
Sakuramoto S (2006) ⁶	Clinical outcomes	Complications	_	Comparisons are made
Doesn't really help – mainly technique oriented	2 patients 2% (2/111) died during follow-up, 1 from peritoneal recurrence at 3 years and 11 months, and one from other causes.	Outcome Total postoperative complications	Rate 12% (13/111)	between different laparascopic procedures rather than with open surgery.
Case series	The remaining patients were alive without recurrence or port site metastasis at a mean	Major outcomes requiring le > 1 month Anastomotic leak	ength of stay of 1% (1/111)	Consecutive patients at one centre
Japan	follow-up of 36 months.	Abdominal abscess Pancreatic leakage	1% (1/111) 1% (1/111)	During the series, the inclusion criterion of tumours < 4 cm in
n = 111	First flatus occurred after a mean period of 2.9 days \pm 1.0days, and first oral intake was achieved after 3.9days \pm 1.0 days.	Cholecystitis (all managed conservatively	1% (1/111) /)	diameter was relaxed to include all tumours not indicated for endoscopic
Study period: Septembert 1998January 2005	The mean length of hospital stay among all the patients undergoing laparascopic gastrectomy	Minor complications Cholecystitis Wound infection	1% (1/111) 3% (3/111)	mucosal resection.
Study aim: To examine surgical outcomes using	was 14.6 days ± 8.7days.	Atelectasis Anastomotic stenosis	3% (3/111) 2% (2/111)	Various comparisons between LADG and hand-assisted laparoscopic surgery, and
different laparoscopic procedures	Operative characteristics The mean operative time was 255 minutes ± 46 minutes.	(endoscopic bougienage) The postoperative course did not differ		between vagus nerve sparing and non vagus nerve sparing surgery are reported but not described here.
Population: Mean age = 59 years. Male = 76%.	Mean blood loss was 147g ± 109g	between the groups by lapa		
Indication: Early gastric cancer	Additional lyphadenectomy was not performed in any patients.			
Technique: Laparoscopic gastrectomy and lymph node dissection with 6-port access, and CO ₂ insufflation to 8 mmHG. 55 patients had 7 cm minilaparotomy, 56 had lymph nodes dissected laparoscopically, including 31 who had celiac branches of the vagus nerve preserved.				
Follow up: Mean 36 months				
Conviction in the second sector	my for cancer	Page 9 of 26		

Study details	Key efficacy findings					Key safety findings		Comments
Kitano S (2007) ⁴	Clinical ou	tcomes				Complications		Potential crossover of patients
	The 5-year disease-free survival (Kaplan-Meier)					Outcome	Rate	with Hosono (2006) and
Case series	was 99.8%					Intraoperative complication	าร	Sakuramoto S (2006) but likely to include additional patients
	IB disease,	and 85.7%	for stage	li disease.		Bleeding	<1% (12/1294)	from other centres.
Japan			una al lia 🗤	10/ /0/400	4) of	Perforation	<1% (1/1294)	
n = 1294	Overall recu patients. Th					Organ injury	<1% (5/1294)	Retrospective case review
11 - 1234	node recurr					Mechanical problem	<1% (4/1294)	
Study period:	liver metast	ases, and 1	skin meta	astasis.		Others	<1% (3/1294)	16 participating centres
April 1994–December 2003						Postoperative complication	าร	
	There were					Bleeding	1% (14/1294)	Conversion to open surgery
Study aim: To examine the short-	patient duri	ng a mediar	n follow up	of 36 mo	nths.	Anastomotic stenosis	3% (38/1294)	was not associated with worse
and long-term outcomes of laparoscopic gastrectomy for early			_			Anastomotic leakage	2% (28/1294)	short- or long-term outcome.
gastric cancer.	-	characteris				Abscess	1% (17/1294)	
	Outcome	LADG	LAPG	LATG	p =	Pancreas injury	1% (14/1294)	Authors state that large prospective randomised
Population: Mean age = 63 years.		(n=1185)	(n=54)	(n=55)		lleus	<1% (3/1294)	studies are required to confirm
Male = 67%.	Operative	, 253.1 ±	229.4 ±	271.4 ±	<0.0	Respiratory complication	<1% (9/1294)	results
Indiantian, Farly goatria concer	time (min)	(19.0)	(31.0)	(26.0)	5	Wound infection	2% (20/1294)	
Indication: Early gastric cancer with adenocarcinomas shown by	p = LATG v	s LADG or	LAPG					
endoscopy and barium meal to be						Overall there were significate		
in the mucosal or submucosal layer of the stomach and not	Conversion				n 1%	intraoperative complication		
candidates for endoscopic	(14/1294) o mechanical					than LAPG or LATG (p<0.0		
resection.	mechanica	problems, v		asun.				
Taskainus Lananaaania								
Technique: Laparoscopic gastrectomy, either distal								
(proximal or distal) or total, and								
lymph node dissection with CO ₂ insufflation, and 5 to 7cm								
minilaparotomy.								
Follow up: Median 36 months								
Conflict of interest: Part supported by government grant								
_, gotonnon grant								
								<u> </u>

IP overview: laparoscopic gastrectomy for cancer

Study details	Key efficacy findings					Key safety findings		Comments	
Tanimura S (2008) ⁸	Operative	character	istics			Complications		No clinical efficacy outcomes	
Case series	Outcome	LAG Circular stapler	Hand assisted Triangular	Total lap	p =	Outcome Intraoperative complication		reported. Laparoscopic technique	
Japan	Operative	239 ±	stapler 212 ± (22)	249 ±	<0.01	Anastomotic leakage Bleeding	<1% (3/586) <1% (1/586)	evolved across the series.	
n = 586	time (min) p = Hand a	(50) Issisted vs	other group	(38) S		Anastomotic stenosis	<1% (1/586)		
Study period:									
March 1998–June 2006									
Study aim: To examine the outcomes of laparoscopic gastrectomy with 'triangulating stapling technique' for early gastric cancer.									
Population: Not reported.									
Indication: Gastric cancer, not otherwise defined.									
Technique: Laparoscopic gastrectomy, either distal (proximal or distal) or total, and intercorporeal anastomosis in 303 patients, with CO_2 insufflation, and 4 to 7cm minilaparotomy.									
Follow up: not reported									
Conflict of interest: Not stated									

Study details	Key efficacy findings	Key safety findings		Comments
Huscher CGS (2007) ³	Clinical outcomes	Complications		Method of case selection or
Case series	Recurrence occurred in 31% (31/100) patients to a mean follow up of 38 months, and 29% (29/100) patients died of recurrence at a mean follow up of 24 months.	Postoperative mortality and me 6% (6/100) and 23% (23/100) Two patients died from respira 4to 6 days follow up. One patie	case accrual not reported. No independent assessment of outcome.	
n = 100	No port site metastases were reported.	congestive heart failure at 57 of patient died of multiple organ f days, one patient died of sepsi following anastomotic leakage	ailure at 78 is at 24 days , and one at	7 patients were lost to follow up suspected to be disease
Study period: Nov 2002 – Sep 2005	The 5-year overall and disease-free survival (Kaplan-Meier) was 59% and 57% respectively,	17 days following a gastrojejur leak.	nostomy	free.
2005	with overall survival ranging from 100% in stage	Outcome	Rate	
Study aim: To report the short-	1A to 9% in stage IV.	Bleeding (surgically treated)	6% (6/100)	
and long-term outcomes of laparoscopic gastrectomy for advanced gastric cancer.	The mean period until first flatus was 3.4 days (range 1 to 7).	Duodenal dehiscence (surgical or conservative treatment)	5% (5/100)	
g		Pneumothorax	1% (1/100)	
Population: Mean age = 66	Operative characteristics	Pancreatitis.	1% (1/100)	
years. Male = 61%.	Conversion to open surgery was required in 3%	Urinary infection	3% (3/100)	
	(3/100) of patients because of bleeding,	Pleural effusion	3% (3/100)	
Indication: advanced gastric cancer with biopsy proven	intestinal adhesions, or tumour invasion of the posterior duodenal wall.	Wound infection	4% (4/100)	
adenocarcinoma. Computed tomography negative for distant metastases.30% of patients had undergone	Lymph node dissection D_1 in 30% of patients and D_2 in 70%.			
previous abdominal surgery	The mean surgical time was 217 minutes (range 120 to 480), and length of stay was 11.4 days			
Technique: Totally Laparoscopic gastrectomy,	(range 6 to 32).			
either partial or total, and lymph node dissection with	The mean clearance margin from the tumour			
CO_2 insufflation. Specimen bag used for removal.	was 6.4 cm (\pm 0.3 cm), and the mean number of lymph nodes dissected was 35 (\pm 18).			
Follow up: Mean 58 months				
Conflict of interest: Not stated				

IP overview: laparoscopic gastrectomy for cancer

Study details	Key efficacy findings	Key safety findings	Comments
Kitano S (2007) ⁷ Kitano is from Oita in Japan – what is he doing writing up a silly case report on botches from Korean surgeons!! - exclude Case report Korea	No efficacy outcomes reported	Complications Case 1 After LADG the colouration of the stomach appeared normal. On the 2 nd postoperative day abdominal pain was aggravated and fever developed Open surgical exploration revealed a blueish gastric remnant, and the pancreatic tail was necrotic with surrounding inflammation.	No details provided of the operator experience or the dominator number of procedures performed at the institution. Few details provided of the exact laparoscopic procedure performed.
n = 2 Study period: Not stated Study aim: To describe two cases with uncommon outcomes		Total gastrectomy, distal pancreatectomy, and splenectomy were performed. Examination showed infarction of the gastric remnant, and severe pancreatitis. Anastomotic leakage and intra-abdominal abscess followed the second procedure. The patient was discharged after 29 days.	Authors postulate that pancreatitis may have led to development or progression of thrombosis of the remnant gastric vessels leading to infarction.
Population: Mean age = 65 years. Male = 50%. Indication: Early gastric cancer Technique: Laparoscopically assisted distal gastrectomy, with Bilroth I reconstruction. No further details provided.		On the 7 th postoperative day abdominal pain increased and fluid drain turned dark. CT showed absence of contrast enhancement at the gastric wall, and the distal pancreas was swollen. Open surgical exploration identified severe pancreatitis, and the distal half of the gastric remnant was blueish, although flow in the splenic vessels and short gastric vessels were preserved.	
Follow up: to 1 month Conflict of interest: Not stated		Total gastrectomy was performed, and the patient recovered on the 13 th day following the second operation.	

Validity and generalisability of the studies

- Some studies included patients treated by laparoscopically assisted surgery, and some by total laparoscopic surgery.
- Insufflation was used in some but not all studies. (irrelevant)
- The degree of resection varied between studies (some patients had total gastrectomy) as did the resection of lymph nodes. This makes comparison between studies difficult.
- Some partial resections involved distal gastrectomy, and others proximal gastrectomy. Expected – depends on site of tumour – exclude this comment)
- Some studies included only patients with early-stage cancer while others were more inclusive, making comparison of outcomes between studies difficult.
- Some studies limited patient inclusion according to lesion size.
- Some studies specified the use of an endoscopy retrieval bag.- is universally used for cancer

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Mr H Ali, Mr M Vipond (Association of Laparoscopic Surgeons of Great Britain and Ireland)

Mr D Menzies, Mr P Sedman (Association of Upper Gastrointestinal Surgeons)

Mr T Dehn, Mr G Fullarton (British Society of Gastroenterology)

- Three including Tom Dehn Specialist Advisers considered this procedure to be a minor variation on an established procedure, and three Advisers said that it was novel and of uncertain safety and efficacy.
- Known adverse events following this procedure include port insertion injury to intra-abdominal organs/vessels, complications of prolonged pneumoperitoneum, anastomotic/duodenal stump leak, chyle leaks, incomplete resection, bleeding and anastomotic stricture.

- Theoretical adverse events may include inadequate lymphadenectomy, cancer seeding, Roux limb ischaemia, deep vein thrombosis, infection and cardiac complications.
- One Adviser thought that the procedure was being taken up in an uncontrolled fashion.
- There is a steep learning curve with this procedure; however, this is the same with any open procedure undertaken for the first time.
- Mentoring should be offered by surgeons experienced in this technique, as the procedure requires advanced laparoscopic skills, and safety is operatordependent.
- The BSG/AUGIS dataset should be collected for each case. ALS, Dendrite database – check with als
- The main controversy in this field is the level of lymph node dissection rather than laparoscopic technique.
- Key efficacy outcomes by which to consider this procedure include mortality (early and late), return to theatre, lymph node clearance and adequate surgical margins.
- Key safety outcomes by which to consider this procedure include anastomotic leak, respiratory complications and hemorrhage.

Issues for consideration by IPAC

- Non-English language studies were excluded.
- Studies including patients with benign gastric tumours were excluded.
- 16 studies (4 RCTs and 12 other comparative studies) are included in the meta-analysis by Hosono (2006)⁵ and have not been included in this overview to avoid 'double-counting' patients.

• Significant number of comparative studies and case series totaling 2223 patients undergoing the laparoscopic procedure are include in appendix A

References

- Ziqiang W, Feng Q, Zhimin C et al. (2006) Comparison of laparoscopically assisted and open radical distal gastrectomy with extended lymphadenectomy for gastric cancer management. Surgical Endoscopy 20: 1738-1743.
- Dulucq JL, Wintringer P, Stabilini C et al. (2005) Laparoscopic and open gastric resections for malignant lesions: a prospective comparative study. Surgical Endoscopy 19: 933-938.
- 3. Huscher CGS, Mingoli A, Sgarzini G et al. (2007) Totally laparoscopic total and subtotal gastrectomy with extended lymph nope dissection for early and advanced gastric cancer; early an long term results of a 100 patient series. The American Journal of Surgery 194: 839-844.
- 4. Kitano S, Shiraishi N, Uyama I et al. (2007) A multicenter study on oncologic outcome of laparoscopic gastrectomy for early cancer in Japan. Annals of Surgery 245: 68-72.
- 5. Hosono S, Arimoto Y, Ohtani H et al. (2006) Meta-analysis of short-term outcomes after laparoscopy-assisted distal gastrectomy. World Journal of Gastroenterology 2: 7676-7683.
- 6. Sakuramoto S, Kikuchi S, Kuroyama S et al. (2006) Laparoscopy-assisted distal gastrectomy for early gastric cancer: experience with 111 consecutive patients. Surgical Endoscopy 20: 55-60.
- 7. Kim HJ, Lee KH, Young KH, et al (2007) Gastric remnant infarction following laparoscopically-assisted distal gastrectomy. CT diagnosis in two cases. Abdominal Imaging 32: 290-292.
- 8. Tanimura S, Higashino M, Fukunaga Y, et al (2008) Intracorporeal Billroth 1 Reconstruction by Triangulating stapling technique after laparoscopic distal gastrectomy for gastric cancer. Surgical Laparoscopic Endoscopy and Percutaneous Techniques 18: 54-58.

Appendix A: Additional papers on laparoscopic

gastrectomy for cancer not included in summary table 2

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies. Studies (of any design) with 20 or less patients undergoing the laparoscopic gastrectomy procedure are not listed here.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non- inclusion in table 2
Adachi Y, Shiraishi N, Shiromizu A, Bandoh T, Laparoscopy-assisted Billroth I gastrectomy compared with conventional open gastrectomy. Archives of Surgery 2000; 135(7):806-810.	NRCT n=102 (49 lap.) FU=36 months	There was no significant difference in complication rate between laparoscopic surgery (8%) and open surgery (21%).	Larger studies are presented in table 2.
Asao T, Hosouchi Y, Nakabayashi T, Haga N, Mochiki E, Kuwano H. Laparoscopically assisted total or distal gastrectomy with lymph node dissection for early gastric cancer. British Journal of Surgery 2001; 88(1):128-132.	Case series n=49 FU= to 6 months	There were no conversions to open surgery, and in 5 cases the macroscopic diagnosis of depth on invasion was found to have been underestimated	Larger studies are presented in table 2.
Azagra JS, Ibanez-Aguirre JF, Goergen M, Ceuterick M, Bordas-Rivas JM, Almendral- Lopez ML et al. Long-term results of laparoscopic extended surgery in advanced gastric cancer: a series of 101 patients. Hepato-Gastroenterology 2006; 53(68):304-308.	Case series n=101 FU=41 months	Actuarial 5 year survival of curative surgery was 34%	A cohort of patients with advanced gastric cancer, some undergoing palliative surgery.
Ballesta LC, Ruggiero R, Poves I, Bettonica C, Procaccini E. The contribution of laparoscopy to the treatment of gastric cancer. Surgical Endoscopy 2002; 16(4):616-619.	Case series n=25 FU=38 months	5 procedures were converted to open surgery. A mean of 30.5 lymph nodes were removed	Larger studies are presented in table 2.
Besozzi A, Besozzi S, Lanza V, Mitolo CI, Novelli D, Sisto T. Laparoscopic treatment gastric cancer with advanced techniques: technical notes and follow-up. Chirurgia Italiana 2007; 59(1):63-67.	Case series n=24 FU=N/S	Complications noted included pleural effusion, subphrenic collection, and partial dehiscence of the duodenal stump.	Larger studies are presented in table 2.
Chiu, P. W. Y. Endoscopic submucosal dissection used for treating early neoplasia of the foregut using a combination of knives. Surgical Endoscopy 22 (3) 777-	Case series n=30 FU= 6months	Successful procedure in 29/30 patients	Larger studies are included in table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non- inclusion in table 2
783.2008			
Dulucq JL, Wintringer P, Perissat J, Mahajna A. Completely laparoscopic total and partial gastrectomy for benign and malignant diseases: a single institute's prospective analysis. Journal of the American College of Surgeons 2005; 200(2):191-197.	Case series n=33 FU=39 months	All resected margins were tumour free. There was one splenectomy, and postoperatively one abscess and one case of delayed gastric emptying.	Larger studies are presented in table 2.
Etoh T, Shiraishi N, Tajima M, Shiromizu A, Yasuda K, Inomata M et al. Transient liver dysfunction after laparoscopic gastrectomy for gastric cancer patients. World Journal of Surgery 2007; 31(5):1115-1120.	NRCT n=205 (147 lap.) FU= 22 to 75 months	The postoperative complication rate was similar between the groups	Largely biochemical rather than clinical outcomes. Studies with longer follow up period are presented in table 2.
Fujiwara M. Longterm Outcomes of Early-Stage Gastric Carcinoma Patients Treated with Laparoscopy- Assisted Surgery. Journal of the American College of Surgeons 2008; 206(1):138-143.	Case series n=94 FU=Up to 5 years	Overall 5 years survival rate was 90%. 3 patients had recurrence including 1 case of port site recurrence.	Larger studies are presented in table 2.
Hiki N, Shimoyama S, Yamaguchi H, Kubota K, Kaminishi M. Laparoscopy- assisted pylorus-preserving gastrectomy with quality controlled lymph node dissection in gastric cancer operation. Journal of the American College of Surgeons 2006; 203(2):162-169	NRCT n=109 (72 lap.) FU= 22 to 75 months	There was no significant difference in the number of lymph nodes retrieved for any of the nodal stations between the groups	Larger studies are presented in table 2.
Huscher CG, Mingoli A, Sgarzini G, Brachini G, Binda B, Di Paola M et al. Totally laparoscopic total and subtotal gastrectomy with extended lymph node dissection for early and advanced gastric cancer: early and long-term results of a 100-patient series. American Journal of Surgery 2007; 194(6):839-844.	Case series n=100 FU= 57 months	3% of operations were converted to open procedures. 5 year disease free survival was 57%	Some cross over / duplication of patients with Huscher (2005) Larger studies are presented in table 2.
Hyodo M. Gasless laparoscopy- assisted distal gastrectomy is feasible and useful for non- obese patients with early gastric cancer. Hepato- Gastroenterology 2007; 54(78):1854-1857.	NRCT n=92 (40 lap.) FU= N/S	3 procedures were converted to open surgery. Blood loss, operative and recovery time were shorter with the laparoscopic approach. No cardiopulmonary complcations	Studies with longer follow up period are presented in table 2.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non- inclusion in table 2
Hyung WJ, Song C, Cheong JH, Choi SH, Noh SH. Factors influencing operation time of laparoscopy-assisted distal subtotal gastrectomy: analysis of consecutive 100 initial cases. European Journal of Surgical Oncology 2007; 33(3):314-319	Case series n=100 FU= to discharge	Multivariate analysis demonstrated that operative time was influenced by BMI score and surgical experience	Studies with longer follow up period are presented in table 2.
Ibanez Aguirre FJ, Azagra JS, Erro Azcarate ML, Goergen M, Rico SP, Moreno Elola-Olaso A et al. Laparoscopic gastrectomy for gastric adenocarcinoma. Long-term results.[see comment]. Revista Espanola de Enfermedades Digestivas 2006; 98(7):491-500.	Case series n=130 FU= 49 months	6 patients died within 60 days of the operation	A mixed cohort of patients some had staging only without resection.
Ishigami, S., Natsugoe, S., Uenosono, Y., Usefulness of sentinel node biopsy in laparoscopic partial gastrectomy for early gastric cancer. Hepato- Gastroenterology 54 (79) 2164- 2166.2007	Case series n=5 FU=?	Average of 2.6 sentinel nodes were detected	Larger studies are included in table 2. Few clinical results of gastrectomy are reported.
Jin SH, Kim DY, Kim H, Jeong IH, Kim MW, Cho YK et al. Multidimensional learning curve in laparoscopy-assisted gastrectomy for early gastric cancer. Surgical Endoscopy 2007; 21(1):28-33.	Case series n=109 FU= to discharge	There were 14 performance and 5 oncologic failures. The learning curve was achieved after 40 patients but was broken when advanced techniques were introduced, or patients were unselected.	Studies with longer follow up period are presented in table 2.
Kim, JJ. Totally laparoscopic gastrectomy with various types of intracorporeal anastomosis using laparoscopic linear staplers: Preliminary experience. Surgical Endoscopy 22 (2) 436- 442.2008.	Case series n=45 FU=?	There was no conversion to an open procedure. First flatus was observed at 2.9 days, liquid diet was started at 3.7 days.	Larger studies are included in table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non- inclusion in table 2
Kim MC, Choi HJ, Jung GJ, Kim HH. Techniques and complications of laparoscopy- assisted distal gastrectomy (LADG) for gastric cancer. European Journal of Surgical	Case series n=128	Postoperative morbidity and mortality rates were 15.6 % and 0.7% respectively.	Studies with longer follow up period are presented in table 2.
Oncology 2007; 33(6):700-705.	FU= 17 months		
Kiyama T, Mizutani T, Okuda T, Fujita I, Yamashita N, Ikeda K et al. Laparoscopic surgery for gastric cancer: 5 years' experience. Journal of Nippon Medical School = Nihon Ika Daigahu Zasshi 2006; 73(4):214-220.	Case series n=101 FU= to discharge	Anastomotic bleeding occurred in 3 patients, pneumohypodermia in 1, remote infection in 6, and stroke in 1 patient.	Studies with longer follow up period are presented in table 2.
Lee JH. A phase-II clinical trial of laparoscopy-assisted distal gastrectomy with D2 lymph node dissection for gastric cancer patients. Annals of Surgical Oncology 2007; 14(11):3148-3153.	Case series n=64 FU= to discharge	The mean number of lymph nodes retrieved was 50.1. There were two conversions to open surgery and complication rate was 3% (2/66).	Larger studies are presented in table 2.
Lee SI, Choi YS, Park DJ, Kim HH, Yang HK, Kim MC. Comparative study of laparoscopy-assisted distal gastrectomy and open distal gastrectomy.[see comment]. Journal of the American College of Surgeons 2006; 202(6):874- 880.	NRCT n=256 (136 lap.) FU=to discharge	Mean operative time was similar and >30 lymph nodes retrieved in each group.	Studies with longer follow up period are presented in table 2.
Miura S, Kodera Y, Fujiwara M, Ito S, Mochizuki Y, Yamamura Y et al. Laparoscopy-assisted distal gastrectomy with systemic lymph node dissection: a critical reappraisal from the viewpoint of lymph node retrieval.[see comment]. Journal of the American College of Surgeons 2004; 198(6):933-938.	NRCT n=431 (89 lap.) FU=N/S	A significantly greater number of lymph nodes were retrieved using the open technique	Few clinical outcomes were reported Studies with longer follow up period are presented in table 2.
Nunobe S. H. Laparoscopy- assisted pylorus-preserving gastrectomy: Preservation of vagus nerve and infrapyloric blood flow induces less stasis. World Journal of Surgery 2007; 31(12):2335-2340.	NRCT n=90 (39 lap.) FU=7 to 21 months	Gastric stasis was observed in 8% of patients in the laparoscopic group and 6% of patients in the open surgery group	Larger studies are presented in table 2.
Ohgami M, Otani Y, Kumai K, Kubota T, Kim YI, Kitajima M. Curative laparoscopic surgery for early gastric cancer: five years experience. World Journal of Surgery 1999; 23(2):187-192.	Case series n=61 FU=23 months	There were 2 recurrences at the site of staple line at 2 years follow up.	Larger studies are presented in table 2.
Orsenigo E., Tomajer. Sentinel node mapping during	Case series	These early gastric cancer patients with nodal	Larger studies are included in table 2.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non- inclusion in table 2
laparoscopic distal gastrectomy for gastric cancer. Surgical Endoscopy 22 (1) 118- 121.2008.	n=34 FU=?	metastases had at least one metastatic lymph node among the SNs identified (sensitivity 100%)	Few clinical results of gastrectomy are reported.
Song, K. Y. Laparoscopy- assisted distal gastrectomy with D2 lymph node dissection for gastric cancer: Technical and oncologic aspects. Surgical Endoscopy 22 (3) 655- 659.2008.	NRCT n=75 (n=44 Lap) FU=?	operative time was significantly longer for the LADG group. The postoperative LOS was significantly shorter for the LADG group (7.7 vs 9.4 days, respectively; $p =$ 0.003). No significant differences were found in the total number of retrieved lymph nodes	Larger studies are included in table 2
Tanimura S, Higashino M, Fukunaga Y, Osugi H. Laparoscopic gastrectomy with regional lymph node dissection for upper gastric cancer. Gastric Cancer 2003; 6(1):64-68.	Case series n=110 FU=to discharge	1% postoperative recurrence.	Studies with longer follow up period are presented in table 2.
Uyama I, Sugioka A, Sakurai Y, Komori Y, Hanai T, Matsui H et al. Hand-assisted laparoscopic function- preserving and radical gastrectomies for advanced- stage proximal gastric cancer.[see comment]. Journal of the American College of Surgeons 2004; 199(3):508- 515.	Case series n=48 FU=24 months	Mean blood loss was 87 ml, and a mean 49.2 lymph nodes were retrieved. There were no instances of recurrence relating to gastric cancer	Larger studies are presented in table 2.
Uyama I, Sakurai Y, Komori Y, Nakamura Y, Syoji M, Tonomura S et al. Laparoscopy- assisted uncut Roux-en-Y operation after distal gastrectomy for gastric cancer. Gastric Cancer 2005; 8(4):253- 257.	Case series n=42 FU=6 moths	There were no conversions to open surgery, and no instances of anastomotic leakage or stricture.	Larger studies are presented in table 2.
Yasuda K. Learning curve for laparoscopy-assisted distal gastrectomy. Digestive Endoscopy 2003; 15(4):280- 283.	Case series n=75 FU=50 moths	The incidence of postoperative complications did not differ between the groups. No conversions to open surgery were required	Larger studies are presented in table 2.

Appendix B: Related NICE guidance for laparoscopic

gastrectomy for cancer

Guidance	Recommendation	
Interventional procedures	None	
Technology appraisals	Imatinib for gastrointestinal stromal tumours.	
	NICE technology appraisal guidance 86 (2004)	
	1.1 Imatinib treatment at 400 mg/day is recommended as first-line management of people with KIT (CD117)- positive unresectable and/or KIT (CD117)-positive metastatic gastro-intestinal stromal tumours (GISTs).	
	1.2 Continuation with imatinib therapy is recommended only if a response to initial treatment (as defined in Section 1.5) is achieved within 12 weeks.	
	1.3 Responders should be assessed at intervals of approximately 12 weeks thereafter. Continuation of treatment is recommended at 400 mg/day until the tumour ceases to respond, as defined in Section 1.5.	
	1.4 An increase in the dose of imatinib is not recommended for people receiving imatinib who develop progressive disease after initially responding (see Section 1.5).	
	1.5 For the purpose of this guidance, response to imatinib treatment should be assessed on the basis of the results of diagnostic imaging to assess size and density of the tumour(s), patients' symptoms and other factors, in accordance with the Southwest Oncology Group (SWOG) criteria detailed in Appendix D. For the purpose of this guidance, response to therapy is defined as the SWOG classifications of complete response, partial response or stable disease.	
	1.6 The use of imatinib should be supervised by cancer specialists with experience in the management of people with unresectable and/or metastatic GISTs.	

Guidance	Recommendation	
Cancer service guidelines	Improving outcomes in colorectal cancer. NICE cancer service guideline CC (2004)	
	High quality surgery can be crucial to patients' survival. Surgery should be undertaken by specialist colorectal cancer surgeons who are members of colorectal cancer multi-disciplinary teams (MDTs) and who can demonstrate low tumour involvement at the margins of the excised specimens, low rates of surgical complications, and high survival rates among their patients.	
Clinical guidelines	Diagnosis and management of colorectal and anal cancer. NICE clinical guideline (in development)	
Public health guidance	None	

Appendix C: Literature search for laparoscopic

gastrectomy for cancer

IP: 677 Laparascopic gastrectomy for cancer		
Database	Date searched	Version searched
Cochrane Library	08/01/2008	Issue 4, 2007
CRD databases (DARE & HTA)	08/01/2008	November/December 2007
Embase	08/01/2008	1980 to 2008 Week 1
Medline	08/01/2008	1950 to December Week 4 2007
Premedline	08/01/2008	January 07, 2008
CINAHL	08/01/2008	1982 to December Week 1 2007
British Library Inside Conferences	08/01/2008	-
NRR	03/01/2008	-
Controlled Trials Registry	08/01/2008	-

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in other databases.

- 1. exp Laparoscopy/
- 2. exp Laparoscopes/
- 3. laparoscop\$.tw.
- 4. or/1-3
- 5. Gastrectomy/
- 6. gastrect\$.tw.
- 7. (gastric\$ adj3 resection\$).tw.

8. or/5-7

9. ((gastric or stomach or gastronintestinal or duodenum or duodenal or digestive tract\$) adj3 (neoplasm\$ or cancer\$ or carcinoma\$ or adenocarcinom\$ or tumour\$ or tumor\$ or malignan\$)).tw.

10. exp Gastrointestinal Neoplasms/

11. 9 or 10

12. 4 and 8 and 11

13. Animals/

14. Humans/

15. 13 not (13 and 14)

16. 12 not 15