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LAPAROSCOPIC SURGERY FOR THE TREATMENT OF COLORECTAL CANCER – REVIEW OF TECHNOLOGY APPRAISAL GUIDANCE No. 17

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1. **EXECUTIVE SUMMARY**

Introduction

Colorectal cancer is a common malignancy in the UK and surgery is the only potential cure. Resection through a laparotomy is the convention but it is associated with pain, complications and long hospital stay. Laparoscopic colorectal surgery was introduced in the early 1990's and previous NICE guidance in 2000 suggested that its use in cancer should only be performed within the context of randomised controlled trials. Since then high quality published evidence with long term follow-up has become available to demonstrate its safety and advantages over open surgery and therefore revision of the original NICE guidance is necessary.

Clinical Effectiveness

Laparoscopic surgery compared with open surgery for colorectal cancer results in less post-operative pain, less use of analgesia, less blood loss, less use of blood products, less short and long term complications, shorter hospital stay and quicker return to usual activities. There is no decrease in the rates of overall survival or disease-free survival, and no increase in the recurrence rate with laparoscopic surgery. Lymph node harvest is the same as open surgery and there is no increase in positive resection margins with laparoscopic surgery. The incidence of port site metastases is less than 1% and is not excessive compared with abdominal wall recurrences in open surgery. Health-related quality of life parameters appear to be similar between the two techniques although current QoL instruments may not be sensitive enough to detect differences.

Cost Effectiveness

The operative costs for laparoscopic resection of colorectal cancer are higher because of longer operating time and the use of more expensive devices. However these costs are offset by shorter hospital stay, less use of analgesia, less use of blood products and less complications in the short and long term. Although the immediate costs to the National Health Service may be higher in laparoscopic than open surgery, overall cost to society remains similar.

Influence of Enhanced Recovery Programmes

The addition of multimodal rehabilitation programme to laparoscopic colorectal cancer surgery may further improve short term recovery and reduce hospital stay. Both methods are complementary to each other and not mutually exclusive. Further high quality, large scale trials are required to determine their individual and combined effects on recovery after laparoscopic colorectal cancer surgery.

Wider Implications to the NHS

Patients are increasingly likely to request minimally invasive surgery for colorectal cancer, particularly when they realise that it is associated with faster recovery without compromising their safety. They should be given the opportunity of undergoing either laparoscopic or open procedures after careful counseling and informed consent.

Conclusions and Recommendations

Laparoscopic colorectal surgery is associated with significant benefits for patients with colorectal cancer. The Association of Laparoscopic Surgeons of Great Britain and Ireland recommends that this technique should be made available to patients outside of randomised trials and that the surgery should be performed by suitably trained laparoscopic colorectal surgeons. Established consultants should undertake a preceptorship programme before embarking on independent laparoscopic colorectal practice. Their results should be carefully audited both in the local hospital multidisciplinary setting and also submitted to the Association of Coloproctology of Great Britain and Ireland colorectal cancer database.

2. **INTRODUCTION**

Colorectal cancer is the second commonest cancer in the UK with an annual incidence of about 36,000 cases and is responsible for 17,000 deaths per year. The only potential cure for colorectal cancer is surgery to remove the primary tumour. The location of the cancer generally determines the segment of the colon and/or rectum to be removed. This may be in the form of right hemicolectomy, left hemicolectomy, sigmoid colectomy, or total colectomy. Cancer of the upper to mid rectum is removed by anterior resection. Low rectal cancers are removed by anterior resection or abdominal perineal excision of the rectum (APER), depending on how close the cancer is to the anal sphincters. If the anal sphincters cannot be preserved without compromising oncological clearance, APER is performed and a permanent colostomy is required. For patients undergoing low anterior resections, total mesorectal excision (TME) is performed to reduce the risk of local recurrence. A temporary diverting ileostomy may also be required if an anastomosis is fashioned to reduce the consequences of an anastomotic leakage.

Surgery for colorectal cancer has traditionally been performed through a relatively long abdominal incision, particularly for simultaneous access to the splenic flexure and to the pelvis in left-sided resections (Motson 2005). Laparoscopic colectomy was first described in the early 1990's (Jacobs 1991; Phillips et 1992) and involves the dissection of tissues around the tumour using laparoscopic instruments inserted through a variable number of laparoscopic ports (ranging from 5 – 12mm in diameter) placed in the abdominal wall. The blood supply to the bowel is divided close to its origin from the aorta, and the tumour

with its draining lymph nodes in the mesentery are then removed out of the abdomen through a short incision. Particular care is taken to have in place a form of wound protection to avoid direct contact between the cancer and abdominal wall during its extraction in order to reduce the risk of cutaneous metastases. Depending on the type of surgery being performed, an anastomosis and/or stoma is fashioned. An anastomosis for a right-sided resection may be performed as a side-to-side anastomosis using a stapling device, or the anastomosis may be handsewn. For a left-sided resection, the anastomosis is usually performed using an anvil inserted into the proximal colon extra-corporeally, and an endoluminal stapling device passed up the anus to complete the anastomosis after re-establishment of the pneumoperitoneum.

All laparoscopic colorectal resections require the removal of the tumour through an incision although most surgeons in the UK perform the dissection intra-corporeally with laparoscopic instruments only (‘laparoscopic’ or ‘laparoscopically-assisted colectomy’). A minority of surgeons uses a hand-port that allows the placement of a gloved hand intra-corporeally whilst maintaining the pneumoperitoneum (‘hand port-assisted laparoscopic colectomy’). The most obvious difference between laparoscopic and open surgery is that the abdominal incisions are much shorter in laparoscopic than those used in open surgery. The longest incision is dictated only by the size of the tumour to be removed.

Although laparoscopic colorectal cancer surgery has been embraced by many surgeons worldwide, not all are persuaded by its benefits. Proponents argue that laparoscopic resection results in less pain, earlier recovery and shorter hospital stay whilst maintaining

similar oncological outcome compared with open surgery. However skeptics challenge that laparoscopic surgery takes longer, has higher operative costs and may expose patients to risks of cutaneous metastases rarely seen in open surgery. Many trials have been published recently on the relative merits of laparoscopic compared with open colorectal surgery. This document aims to review particularly the new evidence published in English that has become available since the original NICE guidance in 2000 (Technology Appraisal No.17 2000). The results from 1 meta-analysis, 18 randomised controlled trials, 27 comparative, non-randomised studies and 32 non-comparative studies are presented.

3. CLINICAL EFFECTIVENESS

Clinical effectiveness is a multi-factorial concept and when comparing a new surgical intervention (laparoscopic colectomy) with a current standard procedure (open colectomy), it is important to establish that the new technology is as safe as the traditional operation. In colorectal cancer surgery, clinical outcome is usually measured directly (overall and disease-free survival) or indirectly using surrogate end-points (time to tumour recurrence, lymph node retrieval and tumour resection margin). Furthermore it is necessary to demonstrate that there are no extra adverse consequences associated with the new technique (cutaneous metastasis, operation duration, blood-loss, short and long term complications). Finally to justify the introduction of the new procedure, factors that may have direct or indirect benefits to the patient needs to be shown (length of hospital stay, pain, recovery time and quality of life).

The most well-established method of comparison between clinical interventions is the randomised, controlled trial (RCT). However large scale surgical RCTs are usually multi-centred involving many surgeons, each contributing relatively few patients into the trial. Standardisation of surgical procedures and expertise is also difficult, particularly involving a new technique with a long learning curve. Therefore expertise-based comparative trials may have greater applicability and feasibility than conventional trials (Devereaux et al 2005). Non-comparative case series are also important in demonstrating clinical outcome from individual surgical units that have acquired expertise in the new technique. Although some studies will have longer post-operative surveillance than

others, all available evidence should be examined on an individual basis as some studies with short follow-ups may contribute important information on short-term results. The following subheadings will be discussed in the context of RCTs in patients with surgically resectable colorectal cancer, supported by non-RCT evidence published in English since 2000.

Clinical effectiveness outcome measures:-

1. Overall survival
2. Disease-free survival
3. Time to tumour recurrence
4. Lymph node retrieval
5. Completeness of resection and margins of tumour clearance
6. The incidence of port site/wound site metastasis
7. Operative duration
8. Blood loss and use of blood products
9. Incidence of short term complications
10. Incidence of long term complications
11. Length of hospital stay
12. Post-operative and long term pain
13. Time to return to usual activities
14. Health-related quality of life

1. Overall survival

Comparative, randomised studies

The first long-term RCT results from a single centre were reported from Barcelona, Spain in 2002 (Lacy et al 2002). Over a five year period, 219 patients with colonic cancer (excluding transverse colon and rectum) were recruited and the median length of follow-up was 43 months. 111 patients underwent laparoscopic resection and 108 patients had open surgery. There was no significant difference in overall survival at five years between those undergoing laparoscopic (82%) compared with open colonic resection (74%; $p = 0.14$). When stratified according to TNM tumour stage, there was no difference in the overall survival ($p = 0.22$) for all stages but laparoscopic colonic surgery for stage III disease had a significant benefit ($p = 0.02$) over open surgery. This difference, at least in part, may have been due to a worse than expected survival in those randomised to open surgery.

The clinical outcomes of surgical therapy study group trial was reported from North America in 2004 (The COST study group 2004). This was a multi-centre RCT trial involving 66 surgeons from 48 institutions, with each surgeon having performed at least 20 laparoscopic colorectal resections and ongoing external quality control of surgical technique and oncological clearance. Over a six year period, 863 patients with colonic cancer (excluding transverse colon and rectum) were eligible for the study and the median follow-up was 4.4 years. 435 patients under went laparoscopic surgery and 428 patients had open colectomy. The overall survival at three years was very similar in

patients undergoing laparoscopic (86%) and open surgery (85%; p = 0.51). There were no significant differences between treatment groups for overall survival for any stage of cancer.

In an RCT from Hong Kong, 403 patients with rectosigmoid cancers were recruited from two institutions (Leung et al 2004) over a nine year period. 203 patients underwent laparoscopic resection and 200 had open surgery. The median follow-up was 50 months. There were no significant differences in overall survival at five years between laparoscopic resection (76.1%) and open surgery (72.9%; p = 0.61), and this similarity was noted when stratified for disease stage.

The MRC conventional versus laparoscopic-assisted surgery in colorectal cancer trial (CLASSIC) has recruited 794 patients with colorectal cancer over seven years from 27 UK centres (Guillou et al 2005). Rectal cancers were included and randomisation was performed at a two-to-one ratio in favour of laparoscopic resection to allow for anticipated conversions to open surgery. Short-term analysis of in-hospital mortality rate has shown no differences between treatment groups and long-term endpoints are awaited.

The European COLOR (colon carcinoma laparoscopic or open resection) included 1248 patients from 27 hospitals over six years. Short-term results will be published later this year.

In another small randomised, controlled trial over a three-year period with a mean follow-up of 4.9 years from New Mexico, USA, overall survival at five years was similar between open and laparoscopically-assisted colonic resection in 43 patients (Curet et al 2000).

Three cancer-related deaths occurred in an RCT of 29 laparoscopic and 20 open colonic resections for cancers after a median follow-up of 35 months (range 3-69 months) from Los Angeles, USA (Kaiser et al 2004). One death was in the open group and one was in the laparoscopic group; the other was in a patient whose operation was converted to open surgery. One death due to primary lung cancer occurred in the open surgery group. At follow-up, 93% of the laparoscopic group (14 of 15 patients) and 95% of the open group (19 of 20 patients) were alive; 85% of the converted group were also alive (11 of 13 patients). At the time of evaluation, 4 patients were alive with cancer, three in the converted group and 1 in the open group.

A small RCT from Tokyo, Japan randomised 59 patients with T2 and T3 colorectal cancers to undergo laparoscopic (29 patients) or open (30 patients) resection over 2 years (Hasegawa et al 2003). The median follow-up was 20 months with no deaths reported in either group.

An RCT from Chengdu, China randomised 171 patients (mean age 44 years) into laparoscopic TME (82 patients) and open TME (89 patients) with anal sphincter

preservation over one year (Zhou et al 2004). After follow-up ranging from 1 to 16 months, no deaths were recorded in either group.

Comparative, non-randomised studies

A prospective, non-randomised, longitudinal cohort study over ten years was conducted to compare laparoscopic versus open resections for colorectal cancers in Orlando, Florida (Patankar et al 2003). 172 patients were recruited into the laparoscopic group and 172 patients into the open group. After a mean follow-up period of 52 months (range 3-128) and with a 100% follow-up data availability, the overall observed five-year survival rate for all stages of colon and rectal cancers was 69% for the laparoscopic group and 64% for the open group ($p = 0.23$). The observed overall 5-year survival rates for the laparoscopic group with a tumour site in the colon were as follows: stage I 76%, stage II 68%, stage III 53% and stage IV 0%. The observed overall five-year survival rates for the open-resection group with a tumour site in the colon were as follows: stage I 80%, stage II 64%, stage III 50% and stage IV 0%. This was not statistically significant ($p = 0.22$). The observed five-year survival rates for the laparoscopic group with the primary tumour in the rectum were as follows: stage I 74%, stage II 70%, stage III 60% and stage IV 0%. The observed five-year survival rates for the open group with the tumour site in the rectum were as follows: stage I 70%, stage II 66%, stage III 50% and stage IV 0%. This was also not significant ($p = 0.09$). The survival rates were also not significantly different ($p = 0.20$) between open and laparoscopic surgery for stage I & II colonic cancers combined. Similarly the survival rates were similar ($p = 0.25$) for stage I rectal cancers (no neoadjuvant treatments) using either surgical technique.

In a prospective, non-randomised trial from Paris, France results from laparoscopic colorectal surgery performed by one surgeon were compared with those from open surgery by another surgeon from the same institution (Champault et al 2002). Over an eight year period, 157 patients were entered into the trial, with 74 undergoing laparoscopic surgery and 83 had open procedure. There was no difference in the overall survival rate between laparoscopic (60.7%) and open (62.5%) surgery over a median follow-up at 60 months. Survival rates were also similar between laparoscopic and open surgery in different disease stages.

A single-institution prospective non-randomised trial from Candiolo, Italy compared laparoscopic (74 patients) and open (181 patients) resection for adenocarcinoma of the left colon or rectum over 5 years, with a median follow-up period of 53 months (Capussotti et al 2004). Overall 5-year actuarial survival was 68.2% for the laparoscopic group and 48.5% for the open surgery group ($p = 0.08$).

In another prospective, non-randomised, controlled trial in an unselected series of patients from Hull, UK with similar study design to the Parisian study, 61 patients underwent a laparoscopic colorectal cancer resection and 53 had conventional open surgery over 3 years (Hartley et al 2000). Crude death rates at a median of 42 months of follow-up were 26/57 in the laparoscopic group (46%) and 24/52 in the open group (46%). These differences were not significant. Stage-for-stage comparison of crude death rates to the limit of clinical follow-up were also not significant. There were no

differences in survival between laparoscopic and open surgery (about 50%) at five years ($p = 0.62$).

In a prospective non-randomised study on a series of 248 consecutive patients undergoing right and left hemicolectomies for cancer in Rome/Ancona, the choice of laparoscopic or open surgery was decided by the patient (Lezoche et al 2002). In the right hemicolectomy group, 55 underwent laparoscopic and 44 underwent open surgery. In the left hemicolectomy group, 86 underwent laparoscopic and 63 underwent open surgery. The mean follow-up was 42 months (range 12-92). Cumulative survival probability at 48 months in laparoscopically resected cases versus open right hemicolectomies was 0.865 vs 0.818. The difference between laparoscopic and open right hemicolectomies did not reach statistical significance in Dukes' B and Dukes' C patients. The cumulative survival probability at 48 months in the group of laparoscopically resected cases versus the open left hemicolectomy cases was 0.971 vs 0.887. The difference between laparoscopic and open right hemicolectomies did not reach statistical significance in Dukes' B and Dukes' C patients. The same authors report a similar study in the same year a smaller cohort (197 patients) who underwent either laparoscopic or open right and left hemicolectomies (Feliciotti et al 2002). The study period, though shorter, was within that of the former report but the follow-up was slightly longer (48.9 months, range 3-8 years). Cumulative survival probability at 48 months in the laparoscopically resected cases versus the open surgery group was 0.892 and 0.867 respectively ($p = 0.51$).

In an extension of the above series by the same authors, 82 laparoscopic right hemicolectomies were compared with 45 open procedures for cancers, the mean follow-up for Dukes' A, B and C patients was 57.3 months (range 12-109) (Lezoche et al 2003). Overall cumulative survival probabilities (CSP) at 72 months in laparoscopically resected cases versus open cases was 0.79 versus 0.76 respectively ($p = 0.32$). The difference of CSP in the 2 groups of patients did not reach significance in Dukes' A (0.87 vs 0.90 respectively, $p = 0.81$), Dukes' B (0.84 vs 0.88 respectively, $p = 0.87$) and Dukes' C (0.72 vs 0.60 respectively, $p = 0.18$) cancers.

In the same study the mean follow-up in the 147 laparoscopic and 71 open left hemicolectomies for cancer for Dukes' A, B and C patients was 57.5 months (range 12-111) (Lezoche et al 2003). Overall CSP at 72 months in laparoscopically resected cases versus open cases was 0.95 versus 0.87 respectively ($p = 0.11$). The difference of CSP in the 2 groups of patients did not reach significance in Dukes' A (1.0 vs 1.0 respectively, $p = 0.93$), Dukes' B (0.96 vs 0.94 respectively, $p = 0.46$) and Dukes' C (0.88 vs 0.70 respectively, $p = 0.07$) cancers.

The Hull group also reported a retrospective analysis of patients undergoing APER laparoscopically (28 patients) and conventionally (61 patients) for rectal cancers over 8 years (Baker et al 2002). The overall survival between the two groups was not significantly different over a median follow-up of 36 months in the laparoscopic group and 27 months in the open group. Mean length of survival in the laparoscopic group was 35.6 months and 30.3 months in the open group ($p = 0.35$). In a study of similar design

from Hong Kong (Leung et al 2000), 59 consecutive patients undergoing laparoscopic (25 patients) and open (34 patients) APER over 3 years were reported. The median follow-up times were 30.1 and 28.3 months respectively. The survival rates at 4 years were 68% for the laparoscopic group and 45.9% for the open group. The difference in survival may have been due more advanced disease in the open cohort. Stage-by-stage comparison for the two groups showed no difference in survival although the number of patients in each disease stage was small.

In a case-control series comparing 144 laparoscopic TMEs versus 144 historical open TMEs from Bordeaux/Marseille, there was no significant difference in the overall survival at 3 years between the two groups (laparoscopic: 89% 3 year survival) after a median follow-up of 18 months (range 1-46) (Bretagnol et al 2005).

A retrospective cohort analysis of laparoscopic (98 patients) and open (219 patients) surgery over 7 years were reported from Hamilton, Canada (Hong et al 2001). Despite a predominance of right-sided lesions in the laparoscopic group, there were no differences in TNM staging between the two groups. There were no statistical differences between laparoscopic and open patients in overall survival ($p = 0.78$) over a mean follow-up of 30.6 months in the laparoscopic group and 21.6 months in the open group.

The Hull group reported a retrospective case control series of 99 patients who underwent laparoscopic (33 patients) or open (66 patients) right hemicolectomy for cancers (Baker et al 2004). With a mean follow-up of 65.7 months, the overall survival was not

significantly different: 40 months in the laparoscopic cohort compared with 39.4 months in the open group (p = 0.34). The trend was maintained when these groups were analysed for node-positive and node-negative tumours.

In a series of 30 laparoscopic and 34 open right hemicolectomy for cancer from Shanghai, the cumulative survival probabilities at 40 months were 76.5% and 74.0% respectively (Zheng et al 2005). No significant difference was found between the two groups (p = 0.85). The mean follow-up was 27.1 months (range 12-40, SD 7.9) for laparoscopic and 26.1 months (range 13-40, SD 7.4) for open surgery (p = 0.63). Three patients (10.0%) died of liver metastases and 1 (3.3%) died of lung metastases, and 2 patients (6.7%) died of other causes not related to colon cancer.

Another institution from Miami reported an observational series of 102 patients who underwent laparoscopic colorectal resections over five years (Lujan et al 2002). The overall survival rate was 64% after a mean follow-up of 64.4 months. The survival rates were 73% for stage I, 61% for stage II and 55% for stage III disease, similar to results obtained in open surgery in 641 historical patients from the same institution (stage I 75%, stage II 65%, stage III 46%) and those reported in conventional surgery on 36,947 cases (stage I 70%, stage II 60%, stage III 44%) during the same period (Jessup et al 1996).

In a retrospective comparison of 20 laparoscopic and 23 open colectomies for Dukes' A cancers from Oita, Japan, no patient died of recurrence during a follow-up period from 13-60 months (mean 36.3, median 38) (Kakisako et al 2000).

In a case-control study of 41 laparoscopic TMEs for rectal cancer compared with a historical 41 cases of open TMEs, four patients died in each group after a mean follow-up of 14 months (range 2-31) but no cancer-related deaths were reported (Breukink et al 2005).

Non-comparative studies

In a prospective multi-centre observational study from the Laparoscopic Colorectal Surgery Study Group (LCSSG) in Germany and Austria, 149 patients underwent laparoscopic APER and 231 patients underwent laparoscopic anterior resection for rectal cancers over a five year period in 23 institutions (Scheidbach et al 2002). Survival rates were similar between APER (86.6%) and anterior resection (71.7%) after a mean follow-up period of 24.8 months. These results compare favourably with previously reported results of open series. Havenga et al found a five-year overall survival rate of 62-75% in an international multi-centre analysis of 1411 patients undergoing conventional TME for primary rectal cancer (Havenga et al 1999). A follow-up study including 190 laparoscopic APERs and 330 laparoscopic anterior resections were reported recently (Scheidbach et al 2004). The overall survival rate was 71.5% (mean follow-up 2.3 years, median 2.1 years). Calculation of the stage-related survival rates revealed a crude survival of 82.0%, 68.8% and 63.3%, respectively for stages I, II and III diseases for a mean follow-up of 2.5, 2.4 and 1.9 years.

The LCSSG also examined the results from 292 patients from 36 hospitals who underwent laparoscopic sigmoid resection for cancer. After a mean follow-up of 2.1 years, the survival rate was 80.9% for the overall patient population and 88.8%, 90.9% and 64.1% respectively for Stages I, II and III disease (Scheidbach et al 2002), similar to those seen in open surgery.

In a prospective observational study from Brisbane, Australia 181 patients undergoing laparoscopic colorectal surgery for cancer over 9 years were examined (Lumley et al 2002). After a median follow-up of 73 months, the five-year survival was 91% for T1 and T2 tumours without nodal metastases, 83% for T3 and T4 tumours without nodal metastases and 74% for nodal metastases (N1 and N2) without distant metastases.

Prospectively collected data from 102 consecutive, unselected patients undergoing laparoscopic TME for rectal cancer over a nine-year period were examined in a single surgeon's practice from Strasbourg, France (Leroy et al 2004). The mean follow-up was 36 months and at five years, the overall survival of all curatively resected patients was 65%, with a mean survival of 6 years.

In a similar study of laparoscopic TME for 100 low and mid-rectal tumours over seven years from Turin & Aosta, Italy, 87 were adenocarcinomas (Morino et al 2003). Survival for 70 patients (80%) with a minimal follow-up of 12 months and a median follow-up of 45.7 months were reported. The 5-year overall survival rate was 74%, with 92% for stage

I disease, 79% for stage II and 67% for stage III, similar to results obtained after open TME (Heald and Ryall 1986).

A case series of 194 unselected rectal cancers were resected laparoscopically from Berlin, Germany over 10 years (Bärlehner et al 2005). Overall survival rate was 90.6% at 1 year, 74.5% at 3 years and 66.3% at 5 years after a mean follow-up of 46.1 (1-128) months. Overall 5-year survival rate was 76.9% after curative resection and 31.8% after palliative resection. At 5 years, the survival rate was 100% for stage I, 94.4% for stage II, 66.6% for stage III and 44.6% for stage IV cancers.

In a prospective series of 80 consecutive unselected laparoscopic TMEs for rectal cancer (52 anterior resections and 28 APERs), the overall survival curve for patients in all stages of cancer showed a 5-year survival rate of 65.1% (CI 52-78.4) after a median follow-up of 31 months (range 0-89) for stages I, II and III disease and 15.5 months (range 4-48) for stage IV disease (Poulin et al 2002). During the follow-up period, 19 deaths occurred: four of unrelated causes and 15 of cancer (0 stage I, 1 stage II, 7 stage III, 7 stage IV). For curative resections (stages I, II and III), the 5-year survival rate was 72.1% (CI 58.4-85.8). The observed survival rate at 5 years was 92.2% (CI 79.4-100) for stage I, 86.7% (CI 69.5-100) for stage II, 53.1% (CI 29-77.4) for stage III and 20% (CI 0-51) for stage IV disease. These results compare favourably with 519 open TME patients reported from Basingstoke (overall 5-year survival 68%; 5-year survival for stages I, II & III 81%) (Heald et al 1998).

A prospective Japanese series from Tokyo reported 70 patients who underwent laparoscopic resection for rectosigmoid and rectal cancers over 8 years (Yamamoto et al 2002). After a median follow-up of 23 months (range 1-94), the extrapolated 5-year survival rate was 100%.

In another single institution series from San Antonio, USA, 50 patients with stage III colorectal cancer were prospectively evaluated (Franklin et al 2000). With a median follow-up of 24 months, overall 3- and 5-year survival was 54.5% and 38.5%, respectively.

A long-term observational study of laparoscopic colectomy for left colonic cancers recruited 206 patients over 5 years from Rennes, France (Lechaux et al 2002). With no patients lost to follow-up and an average post-operative surveillance of 64 months, the overall 5-year survival rate was 79%. Stratified according to disease stage, the 5-year calculated survival was 85% for Dukes' A and B, 61% for Dukes' C and 8% for Dukes' D cancers. The 3-year observed survival rates were 93% for Dukes' A and B, 78% for Dukes' C and 15% for Dukes' D cancers. These data compare favourably with those of the Eurocare Working Group findings: a 3-year survival rate in 11 cancer registries in Europe of 73% for Dukes' A and B, 45% for Dukes' C and 11% for Dukes' D cancers (Gatta et al 2000).

The Japanese group also published a case series of 130 patients with T1 colorectal cancer who underwent laparoscopic resection over 6 years (Watanabe et al 2003). The overall survival at 5 years was 97.9%, consistent with survival rates expected from early cancer.

In a retrospective analysis from New York, USA of 81 patients who underwent laparoscopic colectomies for cancer, the 5-year overall survival rate for the entire group resected with intent to cure (stage I –III) was 77%, with a mean survival of 99.6 months (CI 88.4-110.8) after a mean follow-up of 61 months (Jacob & Salky 2005). When stratified by stage, the observed 5-year overall survival rates for stage I, stage II and stage III were 89%, 65% and 72% respectively. The survival rates for stage II and stage III were equivalent ($p = 0.55$). The Surveillance, Epidemiology, and End Results (SEER) database (SEER Program 2003) for open surgery between the years 1992 and 1999 showed an overall 5-year survival rate of 62.3%. For age group >75 years, the overall 5-year survival rate was 60.5%. The mean age of this study group was 76.3 years. Therefore, the 5-year overall survival in this series compared favourably to the data for the open procedure.

In a series of 55 patients who underwent laparoscopic right hemicolectomy for cancer from Croatia over 10 years, the overall 5-year mortality-free fraction was 63% (Baća et al 2005). The 5-year survival rate in 48 patients without distant metastasis (stage I-III) who had been operated on with curative intent was 75%. 83% of patients with stage I disease were alive after 5 years, compared with none of the 7 patients with stage IV disease surviving longer than 3 years and 8 months ($p = 0.01$).

In a series of 220 patients who underwent laparoscopic rectal cancer resections from Barcelona over 5 years, the mortality after a median follow-up of 18 months (range 1-58) was 16.3% (36 patients, 19 of whom underwent palliative procedures) (Delgado et al 2004). In 29 patients (8.6%), death was disease-related, 26 due to disease progression and 3 during the immediate post-operative period. In 7 patients, death was not disease-related; 2 were due to stokes, one to acute myocardial infarction, one to pneumonia and 3 because of other causes.

In 44 patients with mid or low rectal cancer undergoing laparoscopic TME with construction of a colonic J pouch, the overall actuarial survival rate was 80% at 24 months after a median follow-up of 15 months (range 3-35) (Tsang et al 2003). There were 3 cancer-related deaths and one patient died from an unrelated cause 2 years after operation.

ALSGBI CONCLUSION ON OVERALL SURVIVAL RATE:

LAPAROSCOPIC COLORECTAL CANCER SURGERY ACHIEVES AT LEAST THE SAME LONG-TERM OVERALL SURVIVAL RATE COMPARED WITH OPEN SURGERY.

2. Disease-free survival

Comparative, randomised studies

In the study from Barcelona, the probability of cancer-related survival was significantly higher ($p = 0.02$) in the laparoscopic resection group than in the open surgery group (Lacy et al 2002). For stage III disease, laparoscopic rather than open surgery had a higher probability of cancer-related survival ($p = 0.006$). When the results were analysed based on actual treatment, probability of cancer-related survival ($p = 0.0006$) were significantly higher in patients treated by laparoscopic than open surgery.

In the COST study, the disease-free survival rate was similar ($p = 0.7$) in both laparoscopic and open surgery (The COST study group 2004). These finding held true for patients with any stage of cancer: there were no significant differences between treatment groups in the disease-free survival for any stage.

In the Hong Kong RCT of rectosigmoid cancer, there was no difference ($p = 0.45$) in the disease-free survival at 5 years between laparoscopic and open surgery for stage I-III disease (Leung et al 2004). For rectosigmoid cancers without invasion, no difference ($p = 0.6$) was also found between laparoscopic and open surgery.

In the trial from New Mexico, 4 cancer-related deaths occurred in 18 patients who underwent laparoscopic colonic resection compared with 6 patients out of 18 who died in the open surgery group after a mean follow-up of 4.9 years (Curet et al 2000).

In the RCT of 29 laparoscopic and 20 open colonic resections for cancers from Los Angeles, after a median follow-up of 35 months (range 3-69 months) 90% (18 out of 20 patients) of the open surgery group and 93% (14 out of 15 patients) of the laparoscopic surgery group were alive without disease (Kaiser et al 2004). Of the 13 patients whose operation was converted to open surgery, 8 were alive without disease at evaluation (62%).

Comparative, non-randomised studies

In the prospective trial from Candiolo, laparoscopic surgery for colorectal cancer was identified as a significant prognostic factor for disease-free survival ($p = 0.03$) and cancer-related survival ($p = 0.02$) in multivariate analyses (Capussotti et al 2004). Disease-free actuarial 5-year survivals were 65.2% for laparoscopic surgery and 50.5% for open resection ($p = 0.16$). Cancer-related actuarial 5-year survivals were 76.4% for laparoscopic surgery and 56.0% for open surgery ($p = 0.08$). When actual treatment was analysed to include converted operations in the open surgery group, the difference between laparoscopic and open surgery was more pronounced. Node-positive patients that concluded the operation via laparoscopy had a longer 5-year disease free (73.9% vs 47.8%; $p = 0.056$) and cancer-related (82.1% vs 54.5%; $p = 0.03$) survival.

In a case-control series comparing 144 laparoscopic TMEs versus 144 historical open TMEs from Bordeaux/Marseille, there was no significant difference in disease-free survival at 3 years between the two groups (laparoscopic: 77% 3 year survival) after a median follow-up of 18 months (range 1-46) (Bretagnol et al 2005).

The disease-free survival at 48 months in laparoscopically resected cases versus open right hemicolectomies was 78.3% and 75.8% respectively in the prospective study from Rome/Ancona (Lezoche et al 2002). The disease-free survival rates for laparoscopic versus open left hemicolectmoies were 94.1% and 86.8%, respectively. In their similar report of a smaller cohort of patients during the same study period, the disease-free survival rates at 48 months were 86.5% for laparoscopic and 86.7% for open surgery (Feliciotti et al 2002). In their subsequent series of 82 laparoscopic right hemicolectomies compared with 45 open procedures for cancers, the mean follow-up for Dukes' A, B and C patients was 57.3 months (range 12-109) (Lezoche et al 2003). Disease-free survival at 72 months in laparoscopically resected cases versus open cases was 72.1% versus 73.5% respectively. In the same study the mean follow-up in the 147 laparoscopic and 71 open left hemicolectomies for cancer for Dukes' A, B and C patients was 57.5 months (range 12-111). Disease-free survival at 72 months in laparoscopically resected cases versus open cases was 92.2% versus 87.7% respectively.

In the study from Hamilton, no difference in disease-free survival was found between laparoscopic and open colorectal cancer patients ($p = 0.43$) over a mean follow-up of 30.6 months in the laparoscopic group and 21.6 months in the open group (Hong et al 2001).

Non-comparative studies

The disease-free survival for laparoscopic APER was 62.4% and for laparoscopic anterior resection 54.8% after a mean follow-up of 24.8 months in the LCSSG study (Scheidbach

et al 2002). Testing of the survival function in relation to the two surgical procedures revealed no significant differences. These results are comparable to those obtained with historical conventional surgery (Dixon et al 1991).

Cancer-specific survival of 90 curatively resected rectal cancer patients by laparoscopic TME (excluding stage D at presentation) was 75% at 5 years, with a mean survival of 7.11 years (Leroy et al 2004). Similarly the disease-free survival at 5 years for laparoscopic TME was 63% from the Turin & Aosta trial (Morino et al 2003). The disease-free rate at 5 years was 63%; for stage I it was 92%, stage II 79%, and stage III 42%, similar to those reported in open TME (stage I 94%, stage II 87% and stage III 58%) (Heald and Ryall 1986).

In the series of 194 laparoscopically-resected rectal cancers from Berlin, cancer-related survival rate was 94% at 1 year, 82.4% at 3 years and 78.9% at 5 years after a mean follow-up of 46.1 months (Bärlehner et al 2005). It was 87.7% at 5 years after curative resection and 48.5% at 5 years after palliative resection.

In 44 patients with mid or low rectal cancer undergoing laparoscopic TME with construction of a colonic J pouch, the actuarial disease-free survival rate was 68% at 24 months after a median follow-up of 15 months (Tsang et al 2003).

In the series of 70 patients who underwent laparoscopic resection for rectosigmoid and rectal cancers over 8 years, the expected 5-year disease-free survival rate was 92.1% after

a median follow-up of 23 months (range 1-94) (Yamamoto et al 2002). Two patients (2.9%) developed recurrence of cancer at the anastomotic site, and both underwent salvage re-operation. At the end of the study period, both patients were still alive with no evidence of disease (23 months and 15 months respectively).

In laparoscopic resection for stage III colorectal cancer, cancer-adjusted survival was 91.5% at 1 year, 60.8% at 3 years and 49.1% at 5 years after a median follow-up of 24 months (Franklin et al 2000). Cancer-related deaths occurred in 17 patients (34%). These results were similar to those observed in several large population-based studies: the National Cancer Data Base (Steele 1994), the Surveillance, Epidemiology and End Results Program (Beahrs et al 1992), and the Melbourne Colorectal Cancer Study (Kune et al 1990).

In the retrospective analysis from New York, the 5-year overall disease-free survival rate for the entire group resected with intent to cure (stages I–III) was 73%, with a mean disease-free survival of 96.9 months (CI 85.6-108) (Jacob & Salky 2005). When stratified by stage, the 5-year disease-free survival rates for the three stages were 89%, 59% and 67% respectively. According to the SEER database for open surgery, the overall 5-year cancer-free survival rate for local disease (stages I and II) is 91%, whereas the rate for regional disease (stage III) is 68%. Therefore, the 5-year cancer-free survival rate in this series was no different from that after open surgery.

A German five-centre study examined 399 patients who underwent laparoscopic colorectal cancer resection over six years (Schiedeck et al 2000). In 100 patients who underwent laparoscopic-assisted sigmoid or left colectomy, 92% were free of disease after a mean follow-up of 31.3 months. Overall, 2% suffered a cancer-related death. Concerning 157 anterior resections, 93% were free of disease after a mean follow-up of 26 months. The cancer-related mortality was 1.9% in this group. After a mean follow-up period of 32 months, 91.2% of the 102 patients who underwent laparoscopic APER were free of recurrence. The highest cancer-related death rate of 4.9% was observed in these patients. After a mean follow-up of 30 months, the disease-free survival was 92.5% in 40 laparoscopic right hemicolectomies but there were no cancer-related deaths.

ALSGBI CONCLUSION ON DISEASE-FREE SURVIVAL RATE:

LAPAROSCOPIC COLORECTAL CANCER SURGERY ACHIEVES AT LEAST THE SAME LONG-TERM DISEASE-FREE SURVIVAL RATE COMPARED WITH OPEN SURGERY.

3. Time to tumour recurrence

Comparative, randomised studies

For stage III colorectal cancer, laparoscopic rather than open surgery had a higher probability of being free from recurrence ($p = 0.04$) in the paper by Lacy et al, particularly when results were analysed based on actual treatment ($p = 0.002$).

In the COST study, the one-sided p value for the time to tumour recurrence in favour of the open procedure was 0.83, satisfying the criteria to declare the laparoscopic procedure not significantly inferior to the open procedure (The COST study group 2004). The cumulative incidence of recurrence among patients treated with the laparoscopic procedure did not differ significantly from that for patients who underwent open colectomy (2-sided $p = 0.32$). The estimated difference in the 3-year recurrence-free rate was 2.4 percentage points in favour of the laparoscopic-surgery group.

In the rectosigmoid cancer trial from Hong Kong, the probability of being disease-free at 5 years was not significantly different ($p = 0.45$) between laparoscopic (75.3%) and open (78.3%) surgery (Leung et al 2004). If patients with local invasion were excluded, the probabilities of being disease-free at 5 years were also similar between laparoscopic (76.6%) and open (78.5%) surgery.

No recurrence was noted in 18 patients who underwent laparoscopic colonic resection compared with one patient who developed liver metastases after open surgery in the small RCT from New Mexico (Curet et al 2000).

No laparoscopic patient developed a recurrence in the RCT from Los Angeles (Kaiser et al 2004). In the open surgery group, one patient with stage III disease developed liver metastases; in the converted group, 3 patients found to have stage IV disease were alive with liver, lung, or local recurrence.

Three pelvic recurrences were found in 89 patients who underwent open TME for rectal cancer from Chengdu, China (Zhou et al 2004). Two port-site recurrences were recorded from 82 laparoscopic TME patients.

A study from Sao Paulo, Brazil randomised 13 patients to undergo laparoscopic APER and 15 to undergo open APER (Araujo et al 2003). After a mean follow-up of 47.2 months and with the exclusion of 2 patients in the open APER group who presented with unsuspected synchronous metastasis during surgery, local recurrence was observed in 2 patients in the open group and none in the laparoscopic group.

Comparative, non-randomised studies

In the Orlando study, the incidence of distant metastasis was comparable between laparoscopic and open surgery (Patankar et al 2003). In the laparoscopic group, distant metastsis occurred in 21 patients, giving an incidence of 12.2%, whereas in the open-

resection group, metastases were observed in 18 patients, yielding an incidence of 10.5%, which was not significantly different ($p = 0.61$). The sites of distant metastasis and the number of patients in the laparoscopic group were as follows: liver 12, lung 5, brain 3 and bone 1. The sites of distant metastasis and the number of patients in the open group were as follows: liver 9, lung 5, brain 1, bone 1, retroperitoneum 1 and skin of leg 1. The mean follow-up was 52 (range 3-120) months for the laparoscopic group and 59 (range 3-129) months for the open group. In the laparoscopic group, 82% of patients had a minimum follow-up of 12 months, 71% had a minimum follow-up of 24 months and 60% had a minimum follow-up of 36 months. In the open resection group, these figures were 86, 70 and 62%, respectively. The difference in the incidence of local recurrence was not statistically different between laparoscopic (3.5%) and open groups (2.9%, $p = 0.76$).

In the Parisian trial, recurrent disease developed in 18 of 74 patients in the laparoscopic colorectal cancer group (24.3%) and 21 of 83 in the open surgery group (25%) after a median follow-up of 60 months (Champault et al 2002). Stage-for stage comparison of disease recurrence rates showed no significant differences between laparoscopic and open surgery.

For patients with stage III colorectal cancer, recurrence rate was significantly lower ($p = 0.04$) in laparoscopic surgery (22.2%) than in open resection (49.0%) reported in a non-randomised trial (Capussotti et al 2004).

In the non-randomised trial from Hull, 16 out of 57 (28%) laparoscopic colorectal cancer surgery patients and 11 out of 52 (21%) open surgery patients developed recurrence after a median follow-up of 42 months (Hartley et al 2000). Stage-for-stage comparisons of disease recurrence rates (systemic and local treatment failures) to the limit of clinical follow-up were not significantly different. Pelvic recurrence was identified in 7 patients in the laparoscopic group and 5 patients in the conventional group. The crude local recurrence rate for all cases of rectal cancer was therefore 24% (7 of 29 cases) for the laparoscopic group and 19% (5 of 27 cases) for the open group. Isolated local recurrence without evidence of systemic disease was less frequent and was identified in 1 in the laparoscopic group (3%) and 1 in the open group (4%). These differences between laparoscopic and open groups were not significant.

In the study from Rome/Ancona, the local recurrence rate was lower after laparoscopic surgery in both right hemicolectomies (laparoscopic 5.4% vs open 9%; p = 0.93) and left hemicolectomies (laparoscopic 1.5% vs open 7.5%; p = 0.26) (Lezoche et al 2002). However these differences were not statistically significant. Metachronous metastases rates were similar for both groups (laparoscopic 16.2% vs open 15.1% for right hemicolectomies, p = 0.83; laparoscopic 4.4% vs open 5.7% for left hemicolectomies, p = 0.90). In their similar report, the local recurrence rates were 1.3% for laparoscopic and 2.7% for open hemicolectomies (p = 0.10) (Feliciotti et al 2002). Metachronous metastases occurred in 10.8% of laparoscopic patients compared with 10.7% in open surgery patients (p = 0.56).

In their subsequent series of 82 laparoscopic right hemicolectomies compared with 45 open procedures for cancers, the mean follow-up for Dukes' A, B and C patients was 57.3 months (range 12-109) (Lezoche et al 2003). In the laparoscopic group, 1 Dukes' A patient and 2 Dukes' C patients (7%) developed local recurrence and peritoneal carcinomatosis, 9 patients (1 Dukes' A, 2 Dukes' B and 6 Dukes' C) (20.9%) developed metachronous metastases (6 liver and 3 lung metastases), and 1 more patient (2.3%) died from causes not related to colonic cancer. In the open group 1 Dukes' B patient and 2 Dukes' C patients (8.8%) developed local recurrences, 6 (1 Dukes' A, 1 Dukes' B and 4 Dukes' C) (17.6%) developed liver metastases and 1 more patient (2.8%) died from unrelated causes. No statistically significant difference was observed between the two groups in the local recurrence rate ($p = 0.88$) and in the recurrence of metachronous metastases ($p = 0.99$).

In the same study the mean follow-up in the 147 laparoscopic and 71 open left hemicolectomies for cancer for Dukes' A, B and C patients was 57.5 months (range 12-111) (Lezoche et al 2003). In the laparoscopic group, 3 Dukes' C patients (3.3%) developed anastomotic recurrence, 4 patients (1 Dukes' B, 3 Dukes' C) (4.4%) developed metachronous metastases (3 liver and 1 brain metastases), and 6 more patients (6.6%) died from causes not related to colonic cancer. In the open group 4 patients (1 Dukes' B patient and 3 Dukes' C patients) (7%) developed local recurrences, 3 Dukes' C patients (5.3%) developed liver metastases and 3 more patients (5%) died from unrelated causes. No statistically significant difference was observed between the two groups in the local recurrence rate ($p = 0.56$) and in the recurrence of metachronous metastases ($p = 0.85$).

In laparoscopic versus open APER, the recurrence rate after a median follow-up of 36 months in the laparoscopic group and 27 months in the open group was very similar (Baker et al 2002). The total recurrence rate in the laparoscopic group was 9 of 28 (32.1%) and 23 of 61 (37.7%) in the open group. The isolated recurrence rate was 20 of 61 (32.7%) in the open cohort and 7 of 28 (33.3%) in the laparoscopic group. The mean time to isolated recurrence in the open group was 12.9 months and in the laparoscopic group was 16.8 months. The mean time to distant recurrence in the open cohort was 13.7 months and in the patients who underwent laparoscopy was 21.2 months. These data seemed to illustrate a trend in favour of the laparoscopic cohort, but no statistically significant difference was demonstrated between the two groups.

In the APER study from Hong Kong, the disease-free rates at 4 years (Dukes' D disease excluded) were 84.2% in the laparoscopic group and 77.8% in the open group (Leung et al 2000). 3 of 25 laparoscopic patients (median follow-up 30.1 months) and 5 of 34 open patients (median follow-up 28.3 months) developed recurrences. There was no difference in disease-free interval between the two groups on a stage-by-stage comparison.

In a case-control study of 41 laparoscopic TMEs for rectal cancer compared with a historical 41 cases of open TMEs, no local recurrences were noted in either group after a mean follow-up of 14 months (range 2-31) (Breukink et al 2005). Distant metastases were found in five patients in both groups (2 from Dukes' A, B & C cancers and 3 from Dukes' D cancers in each group).

In the case-control series comparing 144 laparoscopic TMEs versus 144 historical open TMEs from Bordeaux/Marseille, the rate of local recurrence for laparoscopic TME was 1.4% (2 of 144) after a median follow-up of 18 months (range 1-46) (Bretagnol et al 2005). Two patients developed local recurrence at 11 and 28 months after surgery and local control was achieved by pelvic exenteration. Distant metastases rate was 12% (17 of 144). Metastases occurred in the liver in 10 cases, in the chest in 5 cases, in the peritoneum and abdominal lymph nodes in 2 cases.

In a series of 101 laparoscopic rectal excisions from Regensburg, 6 patients presented with distant tumour recurrence during follow-up, predominantly in the liver and lungs (Anthuner et al 2003). Two died of tumour progression and one died of a metachronous lung cancer. Two patients developed local recurrence. No comparative data were presented from the open group of patients.

The recurrence rates were similar ($p = 0.55$) between laparoscopic colorectal cancer surgery (20 of 98 patients; mean follow-up 30.6 months) and open surgery (39 of 219 patients; mean follow-up 21.6 months) in the retrospective analysis from Hamilton (Hong et al 2001).

In the retrospective series of right hemicolectomy from Hull, there were a total of 14 distant recurrences, 3 in the laparoscopic cohort and 11 in the open cohort out of 33 and 66 patients respectively (Baker et al 2004). These recurrences consisted of 8 liver

metastases, 3 widespread peritoneal metastases, and 4 lung metastases, with one of each of these being represented in the laparoscopic group of patients (1 patient in the open cohort had both lung and liver metastases). There were 9 local recurrences isolated in the right iliac fossa (8) or at the anastomosis (1), 4 local recurrences in the laparoscopic cohort (2 in patients who had been converted to open surgery), and five in the open cohort. None of the recurrence rates were statistically significant between the two groups.

In a series of 30 laparoscopic and 34 open right hemicolectomy for cancer from Shanghai, the local recurrence rate was similar (6.7% [2 patients] vs 5.9% [2 patients] respectively) after a mean follow-up of 27.1 months and 26.1 months respectively (Zheng et al 2005). No difference was detected in the metachronous metastasis rate (13.3% [4 patients] vs 14.7% [5 patients]).

The recurrence rate from laparoscopic colorectal resection in the Miami series was 14.7% (15 of 102 patients), including one stage I patient, four stage II patients, nine stage III patients and one stage IV patient (Lujan et al 2002). No comparison with open surgery was reported.

Non-comparative studies

In the LCSSG study, the group of laparoscopic APER had 8 distant metastases (7.1%) and 10 locoregional recurrences (9.0%); the anterior resection group had 22 distant metastases (12.5%) and 9 local recurrences (5.1%) after a mean follow-up of 24.8 months (Scheidbach et al 2002). For laparoscopic sigmoid cancer resection including 214 of 292

patients with at least one follow-up examination, the local recurrence rate was 1.1%, 3.4% and 6%, respectively, for Stages I, II and III disease after a mean follow-up of 2.1 years (Scheidbach et al 2002).

Of 154 potentially curative laparoscopic colorectal resections for analysis, there were 21 cancer recurrences – 16 distant only, 3 local only, 1 local and distant, and 1 port site and distant (13.6% overall recurrence rate) after a median follow-up of 71 months (Lumley et al 2002). Two patients with Australian Clinico-Pathological Staging (ACPS) stage A disease, 8 with stage B disease, and 11 with stage C disease developed recurrences (3.5%, 15% and 26%, respectively). There was a higher incidence of metastatic disease in laparoscopic APER patients (11 of 43 patients) compared with anterior resection and right hemicolectomy. This might have been due to over-representation of advanced cancers in the APER group – more than half of 37 potentially curative APER patients were stage C disease.

In laparoscopic TME for rectal cancer, the overall pelvic recurrence rate was 6% with a mean time to local recurrence of 16.6 months (Leroy et al 2004). This compares favourably with published series of open TME for rectal cancer. Heald et al found an overall 6% rate of local recurrences at 5 years and 8% at 10 years (Heald et al 1998), whilst Hainsworth et al reported an overall recurrence rate of 11% that was stage dependent: 0% for Dukes' A, 8% for Dukes' B, 30% for Dukes' C cancers (Hainsworth et al 1997). Similar results were obtained from the Turin & Aosta trial (Morino et al 2003). The locoregional pelvic recurrence rate was 4.2% (3/70 patients): 3 stage III rectal

cancers at 19, 13, and 7 months post-operatively. There were 3 isolated lung metastases, 10 isolated liver metastases, and 3 multiple metastases after a median follow-up of 45.7 months.

Thirty two recurrences (14.5%) were reported in a series of 220 patients who underwent laparoscopic rectal resections in Barcelona after a median follow-up of 18 months (Delgado et al 2004). There were 12 patients with local recurrence (5.4%) (9 of whom underwent intent-to-cure procedures vs 3 with palliative procedures) and 20 patients (9%) with distant recurrence (15 liver and 5 lung metastases).

Tumour recurrence occurred in 23 of the 145 curatively laparoscopic-resected rectal cancer patients (11.7% distant metastases [3 peritoneum, 5 liver, 9 lung] and 4.1% local recurrence) from the Berlin series after a mean follow-up of 46.1 months (Bärlehner et al 2005). Overall local recurrence rate was 6.7% (4.1% after curative resection and 14.3% after palliative resection).

In 44 patients with mid or low rectal cancer undergoing laparoscopic TME with construction of a colonic J pouch, the actuarial local recurrence rate was 13% at 24 months after a median follow-up of 15 months (Tsang et al 2003). Two patients developed local recurrence, one of whom also had distant metastasis. Five other patients developed distant metastases. Six of the seven patients with recurrent disease initially had a Dukes' C primary tumour. All seven patients had histological evidence of lymphovascular permeation by tumour.

In a prospective series of 80 consecutive unselected laparoscopic TMEs for rectal cancer (52 anterior resections and 28 APERs), the overall local recurrence rate was 3.75% (3 out of 80) for all stages and 4.3% (3 out of 70) for stages I, II and III after a median follow-up of 31 months (range 0-89) for stages I, II and III disease and 15.5 months (range 4-48) for stage IV disease (Poulin et al 2002). All the recurrences took place after laparoscopic anterior resection for stage III disease. For two of these patients, the procedure had been converted to open surgery. These results compare well with 519 open TMEs which had a recurrence rate of 6% (Heald et al 1998).

In stage III colorectal cancer, 20 of 50 patients (40%) developed recurrent disease after laparoscopic surgery and 17 patients eventually died of cancer with distant metastases (Franklin et al 2000). Three patients (6%) had regional recurrences in the pelvis and there were no isolated regional or anastomotic recurrences. The rate and pattern of recurrent disease were similar to those found in open colectomy studies when analysed by stage. Obrand et al reported an overall recurrence rate of 43% in patients with stage III colorectal cancer (Obrand et al 1997).

In laparoscopic surgery for 206 left colonic cancers, recurrence occurred during the first two years in 11 out of the 26 patients (42%) (Lechaux et al 2002). The first recurrence was regional in 25% of cases (anastomosis, abdominal wall, peritoneum) and/or metastatic in 75% of cases (liver, lung bone). Further 6 patients had local recurrence in association with distant metastatic disease.

In the Japanese review of 130 stage I colorectal cancer patients who underwent laparoscopic resection, five developed recurrence (3.8%) after a median follow-up of 61 months (Watanabe et al 2003). The site of recurrence was the liver in 2 patients (1.5%) and local in the three others (2.3%). A patient with rectal cancer developed suture line recurrence 39 months after anterior resection. Another patient with rectal cancer developed recurrence in the lateral pelvic lymph node. One patient with cancer of the descending colon developed recurrence in the regional lymph node 100 months post-operatively.

In 108 patients who underwent laparoscopic colorectal resection in Turin after a median follow-up of 44 months, the probability of tumour recurrence was 13.5%, with one local and three distant metastases during the first 18 months (Degiuli et al 2004).

Two patients (2.9%) developed recurrence of cancer at the anastomotic site after a median follow-up of 23 months from the series of 70 patients who underwent laparoscopic resection for rectosigmoid and rectal cancers over 8 years (Yamamoto et al 2002). The time to recurrence was 39 months and 10 months respectively and both underwent salvage re-operation. At the end of the study period, both patients were still alive with no evidence of disease (23 months and 15 months respectively).

In the New York series of 81 patients who underwent laparoscopic colectomy for cancer, tumour recurrences occurred in 6 patients (8%) (Jacob & Salky 2005). The mean time to remain disease-free (disease-free interval) for those patients resected with intent to cure was 64 months (median 60, range 1-133). Of the six tumours that did recur, the mean time to recurrence was 23 months. There were no anastomotic recurrences. There were no disease recurrences in the stage I patients; however, there was evidence of disease recurrence in 2 of 22 patients (9%) with stage II cancer and in 4 of 19 patients (21%) with stage III disease.

Two local recurrences were reported from a series of 55 patients who underwent laparoscopic right hemicolectomy for cancer (Baća et al 2005). In a Brazilian series of 32 laparoscopic TMEs for rectal cancers, local recurrence was observed in one (3.1%) patient 14 months after surgery (Reis Neto et al 2002). Two (6.3%) patients showed developed hepatic metastases: both with poorly differentiated T3 tumours. In a series of 82 patients with low rectal cancer undergoing laparoscopic TME from Chengdu, China, two patients developed local recurrence one year later, after a follow-up range of 1 to 24 months (Zhou et al 2003).

In the German five-centre study, no local recurrence was noted after a mean follow-up of 31.3 months in 100 patients who underwent laparoscopic-assisted sigmoid or left colectomy but distant metastases were seen in 8 patients (stage I, 0; stage II, 1; stage III, 7) (Schiedeck et al 2000). Concerning 157 anterior resections, after a mean follow-up of

26 months, three patients (stage I, 0; stage II, 1; stage III, 2) had local recurrence and 8 patients (stage I, 0; stage II, 1; stage III, 7) developed distant metastases. After a mean follow-up period of 32 months, local recurrence was documented in 3 patients (stage I, 0; stage II, 1; stage III, 2) and distant metastases occurred in 6 patients (stage I, 2; stage II, 0; stage III, 4) out of the 102 patients who underwent laparoscopic APER. After a mean follow-up of 30 months, no local recurrence but 3 distant metastases (stage I, 1; stage II, 1; stage III, 1) were noted in 40 laparoscopic right hemicolectomies.

In a Brazilian series of 1966 laparoscopic surgery for benign (59.5%) and malignant (40.5%) colorectal diseases, postal questionnaire survey revealed a cancer recurrence rate of 13.8% (91 out of 660 adenocarcinomas) after an average follow-up of 26.5 months (Campos et al 2003). Three parietal recurrences (0.45%) were diagnosed, two at the trocar incision site and one in a patient with disseminated disease.

ALSGBI CONCLUSION ON TIME TO TUMOUR RECURRENCE:

TIME TO TUMOUR RECURRENCE IS NOT SIGNIFICANTLY DIFFERENT BETWEEN LAPAROSCOPIC COLORECTAL CANCER SURGERY AND OPEN SURGERY.

4. Lymph node retrieval

The bowel cancer study from the Association of Coloproctology of Great Britain and Ireland report a median lymph node harvest of 10 (range 0-72) from 6304 resection specimens (Smith et al 2004).

Meta-analysis

In the meta-analysis of 5 trials, no significant difference in the average number of lymph nodes removed with the specimen was noted between laparoscopic and open colorectal cancer resections (Abraham et al 2004). The overall weighted ratio of the number of lymph nodes removed with laparoscopic specimens to those removed with open specimens was 0.98 (n = 412).

Comparative, randomised studies

The same mean number of lymph nodes (11.1) was retrieved from the resected specimens in laparoscopic (SD 7.9) and open (SD 7.4) colorectal cancer surgery in the trial from Barcelona (Lacy et al 2002). Similarly the median number of lymph nodes retrieved was 12 both in laparoscopic and open colonic resection (The COST Study Group 2004). There was no significant difference ($p = 0.18$) in the number of lymph nodes removed between laparoscopic (mean 11.9, SD 7.9) and open (mean 12.1, SD 7.1) rectosigmoid cancer resection (Leung et al 2004). In the MRC-CLASSIC trial, the median lymph node yield was 12 (IQR 8-17) in laparoscopic surgery and 13.5 (IQR 8-19) in open surgery. For T2 and T3 colorectal cancer, the mean number of lymph nodes removed in the laparoscopic resection was 23 (range 7-50) and 26 (range 15-56) in open surgery ($p =$

0.24) (Hasegawa et al 2003). No significant differences were found in lymph node retrieval between laparoscopic surgery (11, range 2-23), open surgery (10, range 1-21) and laparoscopic converted to open surgery (12, 1-29) in colorectal cancer (Curet et al 2000).

No significant differences in the mean lymph node harvest was found in open resection (14, range 3-27), converted operations (16, range 1-32) and laparoscopic surgery (11, range 4-26) in the RCT from Los Angeles (Kaiser et al 2004).

The number of dissected lymph nodes was not significantly different between the 20 laparoscopic and 23 open colectomies for Dukes' A cancers when the two groups were compared for the same level of lymph nodes dissection (D1, 2.7 [range 0-9] vs. 6.0 [range 0-15]; D2, 9.2 [range 5-17] vs. 9.2 [range 2-15]; D3 10.0 [range 6-14] vs. 16.3 [range 5-42]) in the Japanese study from Oita (Kakisako et al 2000).

In a randomised trial on short-term outcome after laparoscopic versus open colorectal surgery for benign and malignant diseases from Milan, Italy, the mean number of lymph nodes collected was 14.8 (SD 7.6) in the laparoscopic group and 14.5 (SD 7.2) in the open group in cancer patients ($p = 0.9$) (Braga et al 2002).

In the Sao Paulo RCT of 13 laparoscopic APERs and 15 open APERs, a mean of 5.5 lymph nodes were harvested in the laparoscopic group compared with a mean of 11.9 nodes in the open group ($p = 0.04$) (Araujo et al 2003).

Comparative, non-randomised studies

No difference was found in the mean number of lymph nodes removed in laparoscopic (13, SD 5.4) and in open (12.5, SD 7.7) colorectal cancer surgery (Champault et al 2002). The mean and median number of lymph nodes retrieved were 12.7 (SD 5) and 12 for laparoscopic resection, and 13.8 (SD 5.7) and 12 for the open resection in the trial from Candiolo ($p = 0.23$) (Capussotti et al 2004).

There were no significant differences in the mean number of lymph nodes harvested between laparoscopic (14.2) and open (13.8; $p = 0.65$) right hemicolectomies and between laparoscopic (9.1) and open (8.6; $p = 0.79$) left hemicolectomies in the study from Rome/Ancona (Lezoche et al 2002). In the follow-up study, the mean number of lymph nodes identified in right hemicolectomy specimens resected by the laparoscopic approach was 14.9 versus 13.8 of the openroup ($p = 0.30$), while that after laparoscopic and open left hemicolectomy was 9.3 and 8.6 ($p = 0.21$), respectively (Lezoche et al 2003).

In APER for cancers, the mean number of nodes harvested in the laparoscopic cohort was 5.2 nodes (SD 3.8) and 5.7 (SD 4.3) in the open cohort ($p = 0.66$) (Baker et al 2002). More nodes were harvested in the APER trial from Hong Kong but there was no difference ($p = 0.34$) in the median number of nodes in laparoscopic APER (10, range 2-31) compared with the open group (12, range 1-41) (Leung et al 2000). There was no significant difference in the mean number of lymph nodes harvested between

laparoscopic (6.9, SD 5.1) and open (6.7, SD 4.4) colorectal cancer surgery in the Hamilton trial (Hong et al 2001). In the study from Hull of right hemicolectomy, there was a mean of 9.8 (median 9; SD 4.19) nodes in the laparoscopic group and 9.6 (median 8; SD 4.59) in the open cohort ($p = 0.59$) (Baker et al 2004). In the Shanghai study of 30 laparoscopic right hemicolectomy, the mean lymph node yield was 11.2 nodes (SD 8.0) compared with 9.7 nodes (SD 6.0) for 34 open procedures ($p = 0.73$) (Zheng et al 2005). There was no difference between the two groups in the yield of epicolic and paracolic nodes ($p = 0.17$), intermediate nodes ($p = 0.22$) and principle lymph nodes ($p = 0.31$).

In a case-control study of 41 laparoscopic TMEs for rectal cancer compared with a historical 41 cases of open TMEs, the median number of lymph node retrieved for each group was 8 (laparoscopic range 1-25, open range 2-20) (Breukink et al 2005). Similar results were reported from a series of 18 laparoscopic and 18 open rectal resections from Nanjing, China (laparoscopic mean 7.8 nodes, SD 1.7, range 4-13 vs open mean 8.2 nodes, SD 2.3, range 3-15; p = non-significant) (Wu et al 2004). More lymph nodes were found in another series of 144 laparoscopic TMEs versus 144 open TMEs from Bordeaux/Marseille (laparoscopic median 10 range 0-42 vs open median 12 range 1-58; $p = 0.03$) (Bretagnol et al 2005). Significantly more lymph nodes ($p < 0.001$) were harvested from 334 open rectal excisions (mean 21.9 nodes, SD 12.9) compared with 101 laparoscopic rectal procedures (mean 15.3 nodes, SD 5.5) in a selective series from Regensburg, Germany (Anthuber et al 2003).

In the Miami series, the mean number of lymph nodes harvested was 6.6 (SEM 0.61, range 0-22) for laparoscopic resection and 7.44 (SEM 0.7, range 0-28) for open surgery (Lujan et al 2002). For stage I disease, the mean number was 4.71 (SEM 0.89) for laparoscopic and 5.33 (SEM 0.92) for open surgery. For stage II, they were 6.69 (SEM 0.94) and 6.99 (SEM 0.94), and for stage III, 9.07 (SEM 1.22) and 9.45 (SEM 1.21), respectively. There were no statistical differences between laparoscopic and open surgery in any disease stages.

In 18 patients who underwent laparoscopic resectional surgery for cancer in Singapore, the mean number of lymph nodes harvested was 11.8 (range 4-21) (Koh et al 2005). This was comparable to the corresponding harvest in the open group of 29 patients, which was 12.2 (range 3-28).

Non-comparative studies

In the LCSSG review, the mean number of lymph nodes investigated was 11.7 (range 0-32) in laparoscopic APER and 13.8 (range 0-52) in laparoscopic anterior resection (Scheidbach et al 2002). In their follow-up study, 'complete' lymph node dissection was reported in 91.9% (174 of 190 patients) of laparoscopic APERs and 87.3% (288 of 330 patients) of laparoscopic anterior resections (Scheidbach et al 2004). It was 'limited' in 6.9% (13 of 190) laparoscopic APERs and in 11.8% (39 of 330) laparoscopic anterior resections. Similar results were obtained in laparoscopic sigmoid resection (mean 13.4), except in stage I disease where a mean of 10.2 (median 9) nodes was removed (Scheidbach et al 2002).

In the laparoscopic TME trial from Strasbourg, the mean number of harvested lymph nodes was 8 (range 0-26) (Leroy et al 2004), slightly less than those in the study from Turin & Aosta (median 12.8, range 6-93) (Morino et al 2003). The mean number of lymph nodes removed from the Barcelona series of 220 laparoscopic rectal resections was 13.8 (SD 2.1, range 5-38) (Delgado et al 2004), similar to those from a Brazilian series of 32 laparoscopic TMEs (mean 12.3 nodes, minimum 8, maximum 18) (Reis Neto et al 2002). The mean number of lymph nodes from the Berlin series of 194 laparoscopic cancer resections was 25.4 (range 11-84) (Bärlehner et al 2005). In a series of 32 laparoscopic intersphincteric resection with coloplasty and coloanal anastomosis for mid and low rectal cancers from Bordeaux, France, the median number of lymph nodes identified in each specimen was 10 (range 0-29) (Rullier et al 2003).

In laparoscopic surgery for stage III colorectal cancer, the mean number of lymph nodes harvested was 21.3 (median 20; range 2-58) (Franklin et al 2000). For laparoscopic left hemicolectomies, the mean number of lymph nodes found was 9.2 (SD 5, range 2-25) (Lechaux et al 2002). The mean number of lymph nodes retrieved in the Japanese series of rectosigmoid and rectal cancers was 14.3 (range 2-39) (Yamamoto et al 2002). In the retrospective series of 81 laparoscopic colectomies from New York, the mean number of lymph nodes in resected specimens was 10.1 (range 1-26) for all stages (Jacob & Salky 2005). No difference was noted between stages I, II and III cancers ($p = 0.2$).

In the German five-centre study that examined 399 patients undergoing laparoscopic colorectal cancer resection, the mean number of lymph nodes removed was 12.1 nodes per procedure (sigmoid or left colectomy 13.1, anterior resection 12.6, APER 11.9, left hemicolectomy 13.5, right hemicolectomy 17.5) (Schiedeck et al 2000).

In an analysis of 536 patients randomised into the COLOR study, a higher number of lymph nodes were harvested at high case volume hospital ($p < 0.001$) (Kuhry et al 2005). In 161 cases from low volume hospitals, the median number of lymph nodes harvested was 9. In 186 cases from medium volume hospitals, it was 8 and in 189 cases from high volume hospitals, the median was 12 lymph nodes.

In a study examining surgical outcomes after laparoscopic colonic surgery in octogenarians, the mean number of lymph node harvested from 17 cancer specimens was 13.6 nodes (range 1-29), compared with 13.3 nodes (range 2-38) in 34 laparoscopic specimens from patients under the age of 60 ($p = 0.79$) (Yamamoto et al 2003).

ALSGBI CONCLUSION ON LYMPH NODE RETRIEVAL:

THE NUMBER OF LYMPH NODES RETRIEVED IS NOT SIGNIFICANTLY DIFFERENT BETWEEN LAPAROSCOPIC COLORECTAL CANCER SURGERY AND OPEN SURGERY.

5. Completeness of resection and margins of tumour clearance

Comparative, randomised studies

The extent of resection was similar in the COST trial (The COST study group 2004). The median proximal margin was 13 cm (range 2-78) for laparoscopic surgery and 12 cm (range 3-50) for open surgery (p = 0.38). The median distal margins were 10 cm (range 2-40) and 11 cm (range 1-42), respectively (p = 0.09). Bowel margins were less than 5 cm in 5% in the laparoscopic group in 6% in the open group (p = 0.52).

For rectosigmoid cancers, the mean distal margin was similar (p = 0.97) between laparoscopic (4.5 cm, SD 3) and open (4.5 cm, SD 2.7) resection (Leung et al 2004).

In the CLASSIC trial (Guillou et al 2005), colonic cancers confirmed by central pathology review showed positive circumferential margins (CRMs) in 6 (5%) of 131 patients allocated to open surgery and 16 (7%) of 246 allocated to laparoscopic surgery, but the difference was not significant (p = 0.45). Positivity rates did not differ when analysed according to actual treatment received. No positive longitudinal resection margins were detected in the open surgery group and only 1 was detected in the laparoscopic group who underwent conversion. Distance of tumour from mesenteric resection margin (surgical high-tie) was similar in both open and laparoscopic surgery groups (median 9 cm, IQR 7-11 vs 8 cm, IQR 6.5-10, respectively). In rectal cancers, positive CRMs were identified in 14 (14%) of 97 patients with open surgery and 30 (16%) of 193 with laparoscopic excisions (p = 0.8). CRM positivity also did not differ

when analysed according to treatment actually received. Of patients undergoing anterior resection, CRM positivity was greater in the laparoscopic than in the open-surgery group (16 [12%] of 129 patients vs 4 [6%] of 64, respectively) but this difference was not significant ($p = 0.19$). For APER, no difference was seen in CRM positivity between laparoscopic (10 [20%] of 49) and open (7 [26%] of 27) groups. Longitudinal resection margins did not differ significantly between treatments ($p = 1.0$). The distance to high tie was slightly higher in the open surgery group (median 14 cm, IQR 10-17) than in the laparoscopic group (median 12 cm, IQR 9-15).

All resection margins were tumour-free in the RCT of laparoscopic versus open colectomy from Los Angeles (Kaiser et al 2004). No significant differences were found among the open, laparoscopic and converted groups with the exception that the specimen was significantly longer ($p < 0.05$) in the open group (mean length 23 cm, range 12-51) than in the laparoscopic group (mean length 19 cm, range 11-23).

No cancer cells were found in resection margins in 82 laparoscopic and 89 open TME specimens in the RCT from Chengdu, China (Zhou et al 2004). The mean distance of the tumour from the section edge was 1.5-3.5 cm for the open group and 1.5-4.0 cm for the laparoscopic group.

Comparative, non-randomised studies

There were no differences in the mean distal resection margin between laparoscopic and open surgery for right hemicolectomy (10.3 cm, SD 6.2 vs 9.8 cm, SD 5.8, respectively),

for left hemicolectomy (7.8 cm, SD 4.5 vs 8.3 cm, SD 4.6, respectively) and for rectal cancer excision (4.2 cm, SD 1.8 vs 3.9 cm, SD 2.4, respectively) in the Parisian study (Champault et al 2002).

All margins were free of tumour invasion at pathology assessment for open and laparoscopic colorectal cancer resection in the trial from Candiolo (Capussotti et al 2004). The mean tumour-free margin was 5.2 cm for laparoscopic and 5.3 cm for open left hemicolectomies ($p = 0.59$) in the study from Rome/Ancona (Lezoche et al 2002).

In the study from Hull, tumour was involving the lateral excision margin in 1 of the 26 laparoscopic APERs where full pathological reports were available and 10 of the 55 open APERs ($p = 0.09$). There was no statistically significant difference in the minimal distance to the lateral margin between the two groups. In the open group ($n = 39$) mean distance to the nearest margin was 3.2 mm (SD 3.4) and in the laparoscopic group ($n = 12$) mean distance to the nearest margin was 4.5 mm (SD 3.9; $p = 0.21$). Similarly, no difference was found between marginal involvement in laparoscopic APER (2 of 25 patients) and open APER (1 of 34 patients) in the trial from Hong Kong (Leung et al 2000).

No difference in distal resection margin was found between laparoscopic (mean 7.2 cm, SD 5.1) and open (mean 7.9cm, SD 10.2) colorectal cancer resection in the study from Hamilton (Hong et al 2001).

Tumour distance from the closest margin was not different for similar procedure and was adequate from an oncological standpoint from the study in Miami (Lujan et al 2002). The tumour distance for laparoscopic and open surgery was:- right (8.85 cm SEM 0.66, range 3-20 vs 8.24 cm SEM 1.23, range 2-24, respectively), transverse (7.50 cm SEM 1.50, range 6-9 vs 8.00 cm SEM 4.00, range 4-12), left/sigmoid (5.66 cm SEM 0.41, range 1.8-12 vs 6.27 cm SEM 0.91, range 2-14), and low anterior resection (4.55 cm SEM 0.44, range 2-7.5 vs 4.21 cm SEM 0.86, range 1.5-8). Tumour distance from the closest margin for APERs did not appear to convey any extra information. Histological examination of the surgical specimens revealed that proximal and distal margins were free of tumour for all patients in both groups.

In a case-control study of 41 laparoscopic TMEs for rectal cancer compared with a historical 41 cases of open TMEs, positive circumferential resection margin involvement (less than 2 mm) was found in 3 laparoscopic (range 1-1.5 mm; 7%) and in 5 open (range 0.5-1; 12%) cases (Breukink et al 2005). The distal resection margin was 35 mm (range 10-100) for laparoscopic and 30 mm (range 5-80) for open TMEs.

In another series of 144 laparoscopic TMEs from Bordeaux/Marseille, 3 (2%) had positive distal margin and 9 (6%) had positive circumferential margin, and a complete microscopic excision (R0 resection) was achieved in 134 patients (93%) (Bretagnol et al 2005). This was not different ($p > 0.05$) from a historical 144 open TMEs from the same institutions (+ve distal margin: 3 [2%], +ve circumferential margin: 8 [6%], R0 resection: 130 [90%]). Distal resection margin was less in the laparoscopic group (median 20 mm,

range 5-80) than in the open group (median 30 mm, range 5-80; $p < 0.01$) but the circumferential margins were similar (laparoscopic median 7 mm, range 0-30 vs open median 8 mm, range 0-20; $p = 0.41$). R0 resection was achieved in 130 open TMEs (90%) and was not different from laparoscopic TME ($p = 0.52$).

No significant differences in the quality of rectal cancer excision were detected between 32 laparoscopic and 43 open rectal cancer excisions from Bordeaux (Rullier et al 2003). In the laparoscopic group, the median distal resection margin was 3 cm (range 0.5-8), and was microscopically negative in 31 patients. The lateral margin was 7 mm (range 0.5-20), and was microscopically negative (more than 1 mm) in 30 of the 32 patients. Complete excision (R0 resection) was achieved in 30 of the 32 patients (one patient had both distal and lateral positive margins). For the open group the median margins were distally 25 mm (range 10-40) and laterally 8 mm (range 1-20); these were not significantly different from the laparoscopic group ($p = 0.50$ and $p = 0.19$ respectively). Complete R0 resection was achieved in 42 out of 43 open resections ($p = 0.57$ compared with laparoscopy).

In a series of 18 laparoscopic and 18 open rectal excisions for cancer from Nanjing, surgical margins were free from tumour in both groups (Wu et al 2004). There was no significant difference in distal rectal margin between the laparoscopic (mean 4.3 cm, SD 1.1) and open (mean 4.6 cm, SD 1.6) groups.

Non-comparative studies

In the LCSSG study, 9 patients (6%) undergoing laparoscopic APER had spontaneous or iatrogenic perforation of the tumour or accidental cutting of tumourous tissue leading to intra-operative tumour cell dissemination, which almost always occurred during the perineal procedure. The mean distal safety margin was 33.6 mm (range 4-145), with 25% of the patients having a clearance less than 30 mm to the resection line (Scheidbach et al 2002). For laparoscopic anterior resections, intra-operative iatrogenic tumour cell dissemination was very low (3 cases - 1.3%). The mean aboral margin of clearance was 3.9 cm (3-165), with 36% of all patients having a clearance of less than 3 cm. In their follow-up study, 'complete' pelvic dissection was reported in 91.9% (174 of 190 patients) of laparoscopic APERs and in 59.7% (197 of 330 patients) (Scheidbach et al 2004). Intra-operative spillage of tumour cell occurred in 6.8% (13 of 190 patients) of laparoscopic APERs and in 1.8% (6 of 330 patients) of laparoscopic anterior resections.

For laparoscopic sigmoid colectomy, the mean distal safety margin was 72 mm (95% CI 15-165 mm; median 65 mm). 47 patients (12.1%) had a distal margin clearance of less than 30 mm, and 12 patients (4%) had less than 15 mm clearance (Scheidbach et al 2002). Intra-operative tumour cell dissemination was reported in 2 patients (0.7%), on both occasions the result of spontaneous tumour perforation.

In the laparoscopic TME study from Strasbourg, a negative distal margin of resection (mean 3.46 cm, range 0.3-10) was found in 90 patients whose resection was considered curative (Leroy et al 2004). Similarly no tumour involvement of the distal and radial

margin was noted in 87 laparoscopic TME cases for cancer (Morino et al 2003). In 2 cases, the distal margin was less than 2 cm (1.3 cm and 1.6 cm). Average distal clearance was 3.4 cm (SD 1.1, range 0.7-11). The mean distance to the distal resection margin was 2.7 cm (SD1.65, range 0.7-8) in the series of 220 laparoscopic rectal dissections from Barcelona (Delgado et al 2004).Of 32 laparoscopic TMEs for rectal cancer from Brazil, no positive resection was found (Reis Neto et al 2002). Distal margins varied from 0.5 to 3 cm.

In 44 patients with mid or low rectal cancer undergoing laparoscopic TME with construction of a colonic J pouch, there was no circumferential margin involvement (Tsang et al 2003). The median distal resection margin was 3 cm (range 0.5-7). One patient had microscopic tumour involvement of the distal resection margin.

In a series of 82 patients with low rectal cancer undergoing laparoscopic TME from Chengdu, China, positive resection margin was found in one patient and the distance of tumour from the section edge ranged from 1.5 to 4 cm (Zhou et al 2003). In another prospective series of 80 consecutive unselected laparoscopic TMEs for rectal cancer (52 anterior resections and 28 APERs), clear distal margins were obtained in all the patients (Poulin et al 2002). However radial margins were not reported consistently.

Adequate margins of resection was reported in all 50 cases of laparoscopic surgery for stage III colorectal cancer resection from San Antonio (Franklin et al 2000). Similarly of 166 patients who underwent curative laparoscopic left hemicolectomy for cancer, no

residual malignancy was detected at the end of the procedure and free excision margins were noted after fixation during the pathologist's examination (Lechaux et al 2002). No positive resection margins were found in 70 laparoscopic rectosigmoid and rectal cancer resections in the Japanese series (Yamamoto et al 2002).

No positive margins were reported in 56 patients who underwent laparoscopic right hemicolectomy from Croatia (Baća et al 2005). The mean width of the tumour-free margins was 6.8 cm (SD 5.3).

In a series of 193 laparoscopic colorectal resections for malignant disease, 93% were for adenocarcinoma (Gibson et al 2000). There were 7 total resection margins of 2 cm or less in sigmoid and left colectomies but all final reports were free of tumour at proximal and distal resection margins. One low anterior resection was converted to APER because of inability to obtain a tumour-free margin.

ALSGBI CONCLUSION ON THE COMPLETENESS OF RESECTION AND MARGINS OF TUMOUR CLEARANCE:

THE COMPLETENESS OF RESECTION AND MARGINS OF TUMOUR CLEARANCE ARE NOT SIGNIFICANTLY DIFFERENT BETWEEN LAPAROSCOPIC COLORECTAL CANCER SURGERY AND OPEN SURGERY.

6. The incidence of port site/wound site metastasis

Comparative, randomised studies

One of the 106 patients who had laparoscopic colorectal resection developed port site metastasis compared with none of the 102 patients who underwent open colectomy in the Barcelona trial after a median follow-up of 43 months (Lacy et al 2002). Tumour recurred in surgical wounds in 3 patients in the COST study after a median follow-up of 4.4 years: 2 of 435 patients in the laparoscopic group and 1 of 428 patients in the open colectomy group ($p = 0.5$) (The COST Study group 2004). No patient developed post site or wound recurrence in either laparoscopic (203 patients) or open (200 patients) rectosigmoid resection in the Hong Kong study after a median follow-up of 52.7 months and 49.2 months, respectively (Leung et al 2004). Similarly, no port site recurrence was noted in laparoscopic colorectal resection for 29 T2 and T3 cancers after a median follow-up of 20 months (Hasegawa et al 2003). No trocar site or wound site recurrences were also noted in the trial from New Mexico after a mean follow-up of 4.9 years of 25 patients (Curet et al 2000). Similarly there were no port-site metastases in the laparoscopic group nor wound recurrences in the converted and open surgery groups after a median follow-up of 35 months in the study from Los Angeles (Kaiser et al 2004).

In the randomised trial from Milan, no port site metastasis was found in 90 patients who underwent laparoscopic cancer surgery (43.3% of patients completing 1 year follow-up) compared with one surgical wound metastasis from 93 cancer patients who underwent open surgery (46.2% completing 1 year follow-up) (Braga et al 2002).

Two port site recurrences were found in 82 laparoscopic TME patients after a follow-up of 1-16 months in the RCT from Chengdu, China (Zhou et al 2004).

Comparative, non-randomised studies

Three wound recurrences (1.7%) were found in the laparoscopic group from the Orlando study (Patankar et al 2003). Of these, two occurred in patients who, on insertion of the laparoscope, were found to have peritoneal seedlings, and the wound recurrences occurred in the conversion to laparotomy incisions. These were considered in the laparoscopic group according to the intention-to-treat analysis. The single instance of port-site/extraction-site recurrence occurred in a stage II colon cancer patient at the 18-month follow-up visit.

Two port site (2.7%) metastases were seen in patients with stage IV and locally advanced carcinoma in the Parisian study of 157 patients with a mean follow-up of 60 months (Champault et al 2002). No isolated port site recurrence developed in any of the 74 patients from the Candiolo study after a median follow-up of 53 months (Capussotti et al 2004). The only case (1.4%) observed was associated with peritoneal carcinomatosis.

In the study from Hull, no port site metastases were detected in the 61 patients undergoing laparoscopic colorectal resection after a median follow-up of 42 months (Hartley et al 2000). However histologically confirmed wound metastases were identified in 3 patients (5.7%) in the open group (53 patients) at a mean of 11 months after resection (range 6-19 months) and a single patient (1.6%) in the laparoscopic group 27 months

after resection. These were not isolated recurrences but instead occurred in the presence of widespread intra-peritoneal disease and were detected at the time of repeat laparotomy.

One port-site recurrence (2.7%) was noted in laparoscopic right hemicolectomy and one (1.5%) in laparoscopic left hemicolectomy after a mean follow-up of 42 months (range 12-92) from the study from Rome/Ancona (Lezoche et al 2002). The one right hemicolectomy port-site recurrence occurred 6 months after a palliative procedure. The left hemicolectomy port-site recurrence occurred in a patient with Dukes' C cancer whose operation was converted to open surgery. The same authors report the same 2 patients with port-site recurrence in 104 patients who underwent laparoscopic colectomy in the same study period (Feliciotti et al 2002) and in another paper consisting of 345 cancers (Lezoche et al 2003).

In laparoscopic versus open APER, no incidences of wound or port site recurrence in either cohort were noted in both the studies from Hull (laparoscopic 28, open 61) (Baker et al 2002) and from Hong Kong (25 laparosopic, 34 open) (Leung et al 2000), after a median follow-up of 36 and 30 months, respectively. Similarly there was no abdominal wall recurrence in a case-control study of 41 laparoscopic TMEs for rectal cancer compared with a historical 41 cases of open TMEs after a mean follow-up of 14 months (Breukink et al 2005), nor in 144 laparoscopic TMEs from Bordeaux/Marseille after a median follow-up of 18 months (Bretagnol et al 2005) and in 101 laparoscopic rectal cancer excisions from Regensburg (Anthuber et al 2003). No port-site recurrence was

reported in a series of 32 laparoscopic rectal resections with coloplasty and coloanal anastomosis to follow-up (Rullier et al 2003).

There were no incisional or trocar site recurrences in laparoscopic colorectal surgery (98 patients) and 3 (1.4%) incisional recurrences in the open group (219 patients) after a mean follow-up of 30.6 months and 21.6 months, respectively (Hong et al 2001). No recurrences occurred in the patients who were converted from laparoscopic to open surgery.

No port site or wound metastases were reported from the case-control study of laparoscopic (33 patients) versus open (66 patients) right hemicolectomy after a mean follow-up of 65.7 months (Baker et al 2004), nor in a similar study of 30 laparoscopic and 34 open right hemicolectomies from Shanghai after a mean follow-up of 27.1 months and 26.1 months respectively (Zheng et al 2005).

One trocar site recurrence in a patient with stage IV disease and 1 extraction site recurrence in a patient with stage II, Dukes' B2 lesion were noted in the series of 102 patients (2%) who underwent laparoscopic colorectal resection in Miami after a mean follow-up of 64.4 months (Lujan et al 2002). However, the one port site recurrence occurred in a patient with carcinomatosis.

No patient had port-site metastasis after laparoscopic colectomy for Dukes' A cancer after a median follow-up of 38 months (Kakisako et al 2000).

Non-comparative studies

No port site recurrences were noted in 149 laparoscopic APERs and 231 laparoscopic anterior resections after a mean follow-up period of 24.8 months in the LCSSG study (Scheidbach et al 2002). Two port site recurrences occurred in 154 potentially curative laparoscopic colorectal resections in the study from Brisbane after a median follow-up of 71 months (Lumley et al 2002). One was in a patient with disseminated disease at the time of surgery and the other in a patient with ACPS C tumour as part of a systemic recurrence. There were no isolated port site recurrences. One patient developed a perineal wound recurrence after a laparoscopic APER. The rectum was inadvertently perforated during dissection and recurrence occurred within 12 months. This was excised and the patient remained well six years after surgery.

No port site recurrence was noted in the laparoscopic TME series from Strasbourg after a mean follow-up of 36 months in 90 potentially curative cases (Leroy et al 2004), compared with a port site metastasis rate of 1.4% (1/70) in the TME study from Turin & Aosta after a median follow-up of 45.7 months (Morino et al 2003). A stage IV rectal cancer presented with a parietal recurrence at the site of the 5 mm trocar positioned in the left flank 17 months after surgery. Similarly no patient presented with port site metastasis after a median follow-up of 18 months from 220 laparoscopic rectal resections in Barcelona (Delgado et al 2004), nor in the Brazilian series of 32 laparoscopic TMEs (Reis Neto et al 2002) and in a series of 44 laparoscopic TMEs with colonic J pouch reconstruction after a median follow-up of 15 months (Tsang et al 2003). Port-site

metastases occurred in one patient (0.5%) out of 194 laparoscopic rectal resections for cancer in the Berlin series after a mean follow up of 46.1 months (Bärlehner et al 2005). No port site recurrence was reported from a series of 82 patients who underwent laparoscopic TME with anal sphincter preservation after a follow-up ranging from 1 to 24 months from Chengdu (Zhou et al 2003), nor in 80 laparoscopic TMEs after a median follow-up of 31 months for stages I, II and III disease (Poulin et al 2002). No port site recurrence was reported from a series of 372 laparoscopic procedures for malignant colorectal diseases by the same group of surgeons (Schlachta et al 2003).

In laparoscopic colorectal surgery for 50 stage III cancers, no trocar site implants were observed after a median follow-up of 24 months (Franklin et al 2000). In the study of 206 laparoscopic left hemicolectomies after a median follow-up of 65 months, one patient (0.6%) had an abdominal wall recurrence at the site of mini-laparotomy 7 months after surgery (Dukes' C tumour) associated with hepatic and peritoneal recurrence (Lechaux et al 2002).

No port site recurrence was observed in laparoscopic colorectal surgery for 130 stage I cancers after a median follow-up of 61 months (Watanabe et al 2003), nor in the study of 56 cancer patients after a median follow-up of 44 months (Degiuli et al 2004). Similarly no port sites or wound recurrences were found in the Japanese series of 70 laparoscopic rectosigmoid and rectal cancer resections after a median follow-up of 23 months (Yamamoto et al 2002). Among patients with disease recurrence in the retrospective New

York study, there were no port-site recurrences and no peritoneal seeding after a mean follow-up of 61 months (Jacob & Salky 2005).

In the German five-centre study that examined 399 patients undergoing laparoscopic colorectal cancer resection after a mean follow-up of 30 months, one trocar site recurrence was seen in an 84-year old female, which occurred 24 months after sigmoid resection for a stage III cancer (Schiedeck et al 2000).

Two trocar site recurrences were reported after an average follow-up of 26.5 months in a series of 660 adenocarcinomas excised laparoscopically from a postal survey of 16 Brazilian surgical teams who performed a total of 1966 laparoscopic colorectal procedures for benign and malignant diseases (Campos et al 2003).

In a series of 193 laparoscopic colorectal resections for malignant disease, 93% were for adenocarcinoma (Gibson et al 2000). Recurrence of cancer at a port site or incision was higher in the converted group, with an implantation rate of 1.8%, compared with 0.7% in those completed laparoscopically.

In the Italian Registry of Laparoscopic Colorectal Surgery database, 1189 patients with colonic cancer and 564 patients with rectal cancer were enrolled over eight years (Silecchia et al 2002). A total of 20.8% of the cancer patients were lost to follow-up. At a median follow-up of 51 (range 6-113) months, 16 patients (0.9%) developed abdominal wall recurrences. Ten patients presented in an advanced stage (III for 7 patients and IV

for 3 patients). Eleven cases occurred during the learning curve period (the first 50 consecutive cases). The median survival time after diagnosis of abdominal wall recurrences was 16 (range 12-60) months.

ALSGBI CONCLUSION ON THE INCIDENCE OF PORT SITE/WOUND SITE METASTASIS:

THE INCIDENCE OF PORT SITE/WOUND SITE METASTASIS AFTER LAPAROSCOPIC COLORECTAL CANCER SURGERY IS LESS THAN 1%, AND IS NOT SIGNIFICANTLY DIFFERENT COMPARED WITH OPEN SURGERY.

7. Operative duration

Meta-analysis

In a meta-analysis of 12 trials reporting a total of 1055 patients, laparoscopic resection for cancer took a mean of 32.9% (range 20.3-60.0) longer to perform than conventional open resection (Abraham et al 2004).

Comparative, randomised studies

Operative duration was significantly longer ($p = 0.001$) in laparoscopic colorectal resection (mean 142 mins, SD 52) compared with open surgery (mean 118 mins, SD 45) in the Barcelona trial (Lacy et al 2002). Similarly surgery times were significantly ($p < 0.001$) prolonged in laparoscopic colectomy (mean 150 mins) compared with open resection (mean 95 mins) in the COST study (The COST study group 2004). This difference ($p < 0.001$) was also found in laparoscopic rectosigmoid resection (mean 189.9 mins, SD 55.4) compared with open surgery (144.2 mins, SD 57.8) in the Hong Kong trial (Leung et al 2004).

In the MRC-CLASSIC trial, duration of operation was shorter in open surgery than in laparoscopic surgery (Guillou et al 2005). On an intention-to-treat basis, the median anaesthetic time for open surgery was 135 mins (IQR 100-180) whereas that for laparoscopic surgery was 180 mins (IQR 135-220). The results were similar when analysed according to the actual treatment received.

In a subset of patients undergoing the COLOR trial that compared the costs of laparoscopic and open colectomy for cancers, the time in the operating room was 155 mins (CI 146-165) for 98 laproscopic resections and 122 mins (113-131) for 112 open operations (Janson et al 2004). The duration of anaesthesia was longer in the laparoscopic cohort (232 mins, CI 219-245) compared with the open group (184 mins, 172-196) but less time was spent in recovery room: 443 mins (371-516) and 564 mins (497-632), respectively.

Laparoscopic colorectal resection (mean 275 mins, range 184-410) for T2 and T3 cancers took significantly longer ($p < 0.0001$) to perform than open surgery (mean 188 mins, range 127-272) (Hasegawa et al 2003). Similarly operative times were significantly longer ($p < 0.001$) for 37 laparoscopic resections (148 mins, SD 47) than 46 open resections (101 mins, SD 50) for cancer in the trial from St. Louis, USA (Winslow et al 2002). The operating room time was also significantly longer ($p < 0.05$) for laparoscopic colectomy for cancers (mean 210 mins) than for open surgery (mean 138 mins) in the trial from New Mexico (Curet et al 2000).

The median operating times on an intention-to-treat basis were similar for 118 laparoscopic resections (88 mins, range 15-220) and 118 open resections (70 mins, 20-195) for colorectal cancers in an RCT assessing the effect of surgery on systemic immunity from Singapore (Tang et al 2001). Fifteen patients underwent conversion to open procedure and the median operating time for these patients was 110 mins (range 50-220), compared with 85 mins (range 15-190) for those who did not have conversion.

In the study from Los Angeles, the mean operative time was significantly shorter ($p < 0.05$) in open surgery (65 mins, range 45-125) than in laparoscopic colonic resection (125 mins, range 70-155) (Kaiser et al 2004). The mean operative time for the converted group (125 mins, range 80-270) was similar to laparoscopic group.

In the RCT from Chengdu, China, the respective mean operating times for laparoscopic and open procedures were 120 mins (range 110-220) and 106 mins (range 90-230). This was not statistically different between the two groups ($p = 0.05$) (Zhou et al 2004).

In the Sao Paulo RCT of 13 laparoscopic APERs and 15 open APERs, mean operation time was 228 mins for the former and 284 mins for the latter ($p = 0.04$) (Araujo et al 2003). Mean anaesthesia duration was shorter ($p = 0.03$) for laparoscopic when compared with open APER (304 mins vs 362 mins respectively).

A smaller RCT examining the effect of cancer surgery on peritoneal fibrinolytic capacity reported a longer duration of operation for 14 laparoscopic colorectal resections (median 205 mins, range 120-260) than 16 open operations (median 165 mins, 100-285) (Neudecker et al 2002).

In the randomised trial of resection for benign and malignant colorectal diseases from Milan, the operative time was longer ($p = 0.001$) in the laparoscopic group (136 patients; mean 222 mins [SD 74]) than in the open group (133 patietns; 177 mins [SD 56]) (Braga

et al 2002). The same authors report in the same year similar differences in operative times in a smaller group of patients (40 laparoscopic and 39 open resections) undergoing a randomised trial examining metabolic and functional results after surgery (Braga et al 2002). It is unclear whether this cohort represents a subset of patients from the former study.

In the RCT examining the functional recovery after colonic resection for benign and malignant diseases, the operative time was significantly longer ($p < 0.05$) in the 30 laparoscopic cases (median 215.5 mins, range 100-363) than in the 30 open cases (median 131.5 mins, range 79-234) (Basse et al 2005).

Comparative, non-randomised studies

In the Parisian study, the mean operating time was significantly longer ($p = 0.006$) in the laparoscopic group (144.7 mins, SD 38.5) than in the open conventional study group (124.6 mins, SD 52.6) (Champault et al 2002). The operation time was significantly shorter ($p < 0.001$) in open APER (mean 166.3 mins, SD 36.3) compared with laparoscopic APER (mean 215.6 mins, SD 47.9) (Leung et al 2000). However no difference ($p = 0.90$) in operative time was found between 101 laparoscopic rectal excisions (mean 217.9 mins, SD 70.9) compared with 334 open procedures (mean 218.9 mins, SD 74) in a selective series from Regensburg (Anthuber et al 2003).

Operating time was significantly longer ($p < 0.001$) in 32 laparoscopic rectal resections (median 420 mins, range 300-600) with coloplasty and coloanal anastomosis for mid and

low rectal cancers than in open surgery (median 322 mins, range 210-390) (Rullier et al 2003). For the former group, a median of 300 mins was required for the laparoscopic procedure and 120 mins for the perineal procedure.

In a case-control study of 41 laparoscopic TMEs for rectal cancer compared with a historical 41 cases of open TMEs, the total operative time was longer in the laparoscopic group (median 200 mins, range 120-335) than in the open group (median 180 mins, range 110-260) although this did not reach significance ($p = 0.05$) (Breukink et al 2005). Laparoscopic low anterior resection (median 195 mins, range 120-290) was significantly longer ($p = 0.03$) to perform than open surgery (median 170 mins, range 110-250). There was no difference in operating time for laparoscopic (median 225 mins, range 135-335) versus open APER (median 225 mins, range 150-260; $p = 0.46$).

The mean operating time was significantly longer ($p < 0.05$) in 18 laparoscopic rectal cancer excisions (mean 189 mins, SD 18) than 18 open procedures (mean 146 mins, SD 22) (Wu et al 2003).

The mean operative time was significantly longer ($p = 0.03$) in laparoscopic (190 mins, range 90-330) than in open (140 mins, range 90-280) right hemicolectomies (Lezoche et al 2002). Similarly laparoscopic (240 mins, range 150-480) left hemicolectomy took longer to perform ($p = 0.04$) than open surgery (190 mins, range 130-340). In their follow-up series, the mean operative time was still longer in laparoscopic (182 mins, range 90-330) than in open (140 mins, range 90-280) right hemicolectomies but this was

not significant (p = 0.05) (Lezoche et al 2003). Laparoscopic left hemicolectomy took longer to perform than open surgery but this was also not significant (mean 222 mins, range 105-480 vs 190 mins, range 130-340, respectively; p = 0.30). The operating time decreased in the last 50 patients compared with the first 50 patients for both laparoscopic right hemicolectomy (mean 150 mins, range 90-240 vs mean 201 mins, range 140-330) and laparoscopic left hemicolectomy (mean 192 mins, range 105-320 vs mean 249 mins, range 150-480).

No difference was found in the operating time between open colorectal resection (mean 129 mins, SD 53.5) and laparoscopic surgery (mean 140 mins, SD 49.5) in the study from Hamilton (Hong et al 2001). Similarly, the anaesthetic time was not different (p = 0.15) for laparoscopic (mean 107.2 mins, median 107 mins, SD 40) and open (mean 97.4 mins, median 90 mins, SD 34.2) right hemicolectomy (Baker et al 2004). Mean operation time for laparoscopic and open right hemicolectomy from Shanghai was 152.6 mins (SD 28.2) and 147.2 mins (SD 27.5) respectively (p = 0.56) (Zheng et al 2005).

There was no difference in the operation time in 20 laparoscopic colectomies (mean 214 mins, range 125-345) compared with 23 open colectomies (mean 228 mins, range 110-375) in the Japanese study of Dukes' A cancers (Kakisako et al 2000).

The mean operative time for 35 laparoscopic colorectal operations for benign and malignant diseases was 146 mins (range 15-315) compared with 125 mins (range 40-245)

in 42 open procedures (p = 0.17) (Koh et al 2005). In 7 converted patients, the mean operative time was 154 mins (range 105-200).

In a series of 338 laparoscopic colorectal resections for benign and malignant diseases, the actual operating time was 190 mins for successful laparoscopic procedures, which was 35 mins longer than those whose surgery was converted (Gibson et al 2000).

The duration of surgery was about 60 mins longer in laparoscopic surgery (mean 232 mins, SD 43) compared with open surgery (mean 173 mins, SD 37) in a blinded prospective study of the incidence of DVT colorectal resection for benign and malignant diseases (Mall et al 2001).

Non-comparative studies

The mean duration of operation was 221 mins (CI 110-345) for laparoscopic APER and 200 mins (CI 93-339) for laparoscopic anterior resection in the LCSSG study (Scheidbach et al 2002). In their follow-up study, the mean duration was 218 mins (SD 71) and 204 mins (SD 195) respectively (Scheidbach et al 2004). This was less for laparoscopic sigmoid resection (mean 172 mins, CI 85-300) (Scheidbach et al 2002).

For laparoscopic TME, the mean operating time ranged from 202 mins in the Strasbourg study for rectal cancers (Leroy et al 2004) to 250 mins (SD 31.2, range 110-540) in the series from Turin & Aosta for benign and malignant tumours (Morino et al 2003). The mean operative time was 178.5 mins (SD 55.8, range 65-320) in the Barcelona series of

220 laparoscopic rectal dissections (Delgado et al 2004) and 174 mins in the Berlin series of 194 laparoscopic rectal excisions (Bärlehner et al 2005). Similarly the median operating time was 180 mins (range 135-300) in series of 44 laparoscopic TMEs from Hong Kong (Tsang et al 2003). The mean operating time for 82 laparoscopic TMEs with anal sphincter preservation from Chengdu was 120 mins (range 110-220) (Zhou et al 2003).

In a prospective series of 80 consecutive unselected laparoscopic TMEs of rectal cancers (52 anterior resections and 28 APERs), there was no difference in the operating times for anterior resection and APER (median 205 mins, SD 63 vs median 210 mins, SD 35; $p = 0.39$) (Poulin et al 2002).

In the retrospective New York series of 81 laparoscopic colectomies for cancer, the median operating time was 182 mins (mean 185, SD 51, range 80-365) (Jacob & Salky 2005). The mean operating time for a series of 56 laparoscopic right hemicolectomies for cancer from Croatia was 119 mins (SD 38) (Baća et al 2005). For left hemicolectomy for cancer, the mean operative time was 150 mins (SD 40) (Lechaux et al 2002).

In a 2-year study of 120 laparoscopic colectomy and 31 laparoscopic low anterior resection for cancers from Tokyo, Japan, the median operating time was significantly longer ($p < 0.0001$) in the anterior resection (250 mins, range 190-472) than in colectomy (200 mins, range 115-348) (Yamamoto et al 2004).

In the German five-centre study that examined 399 patients undergoing laparoscopic colorectal cancer resection, the mean duration of surgery was 176 mins for sigmoid or left colectomy, 235 mins for anterior resection, 257 mins for APER and 146 mins for right hemicolectomy (Schiedeck et al 2000).

The median duration of operation in 39 elderly or high-risk patients with benign or malignant diseases in whom a laproscopic colonic resection was completed was 180 mins (range 120-270) (Bardram et al 2000). Similarly no difference ($p = 0.12$) was found in the operative time between laparoscopic surgery for 17 octogenarians (mean 177 mins, range 113-235) compared with laparoscopic surgery for 34 patients under 60 years old (mean 199 mins, range 110-335) (Yamamoto et al 2003). The anaesthesia time was also similar between the two groups (mean 263 mins, range 173-352 vs mean 274 mins, range 184-400; $p = 0.46$). In a series of 181 laparoscopic sigmoid colectomies for benign and malignant conditions, the mean operative time was 119 mins (SD 35) (Senagore et al 2003).

The mean operative time for 150 laparoscopic colorectal resections for benign and malignant conditions (52 curative and 17 palliative) was 169 mins (range 45-413) (Lauter & Froines 2001). Mean operative times for successfully completed laparoscopic procedures was 164 mins (range 45-413). Mean operative time for converted procedures was 203 mins (range 70-318). Mean operative time for laparoscopic right hemicolectomy was 121 mins (range 70-195), and for sigmoid resections it was 177 mins (range 45-358).

In the LCSSG study of 4834 patients with benign and malignant colorectal diseases undergoing laparoscopic surgery, 1668 (34.5%) were for malignancies (Rose et al 2004). The average operating time was 171.4 mins. The longest average operating time was seen for anterior resection at 214.5 mins (range 55-520). The shortest average operating time was associated with the construction of a colostomy at 76.8 mins (range 20-246). During the course of the study, a continual decrease in operating times was observed as a reflection of the learning curve.

In the study of benign and malignant colorectal diseases from Turin, the mean operating time was 183 mins (CI 160-305) (Degiuli et al 2004). Patients were divided chronologically into 3 groups (G1 = first 35 patients, G2 = second 35 patients and G3 = last 38 patients). The longest operation was the total abdominal colectomy (305 mins), followed by anterior resections (mean 198 mins, CI 185-234) and right hemicolectomy with intracorporeal division of blood supply (mean 190 mins, CI 181-205). The mean operating time for left or sigmoid resections was 175 mins (CI 150-196). The mean operative time was shorter in G3 (171 mins) compared with G1 (208 mins) and G2 (196 mins).

In a prospectively collected series of benign and malignant laparoscopic colorectal resections from Toronto & Quebec, operating time was longer for the first 30 cases than for the next 31-60 cases, 61-90 cases, 91-120 cases and 121 or more cases (Schlachta et al 2001). Moreover there was a significant decline ($p < 0.001$) in operating time comparing early experience (1^{st} 30 cases: median 180 mins) with late experience (more

than 30 cases: median 160 mins), despite an increase in more difficult operations (males and rectal resections) performed in later stages. The same surgical groups reported a series of 750 attempted laparoscopic colorectal procedures (malignancy accounted for 49.6% of cases) of which 669 were completed laparoscopically (Schlachta et al 2003). The overall median operating time was 175 mins (range 50-450). For segmental resections only, the operating time was longer for procedures converted to open surgery than those completed laparoscopically (median 212 mins vs 165 mins, $p < 0.001$).

Similarly in the analysis of 536 patients randomised into the COLOR study, the median skin-to-skin time for laparoscopic colon resections was 160 mins at low case volume hospitals, 153 mins at medium case volume hospitals, and 130 mins at high case volume hospitals (Kuhry et al 2005). For this reason, low and medium caseload hospitals reported significantly longer skin-to-skin times than to high volume hospitals ($p < 0.001$). Median time in the operating theatre was 240 mins for laparoscopic colon resection at hospitals with a low case volume versus 210 mins at medium case volume hospitals and 188 mins at high case volume hospitals. All comparisons of low, medium and high case volume hospitals showed significant differences in total time spent in the operating theatre ($p < 0.001$).

ALSGBI CONCLUSION ON OPERATIVE DURATION:

LAPAROSCOPIC COLORECTAL CANCER SURGERY REQUIRES MORE OPERATING TIME COMPARED WITH OPEN SURGERY, ALTHOUGH THIS

DECLINES WITH INCREASING LAPAROSCOPIC EXPERIENCE OF THE SURGEON.

8. Blood loss and use of blood products

Meta-analysis

In a meta-analysis of 12 trials of 1055 patients, the incidence of significant haemorrhage requiring a blood transfusion was lower in the laparoscopic resection group (8 events out of 537) than open surgery (13 events out of 518) but the difference was not statistically significant (odds ratio 0.71, CI 0.33-1.54, p = 0.38) in both fixed effects model and random effects model (Abraham et al 2004).

Comparative, randomised studies

Intra-operative blood loss was significantly lower (p = 0.001) in laparoscopic colectomy (105 mls, SD 99) than in open surgery (193 mls, SD 212) in the Barcelona trial (Lacy et al 2002). Laparoscopic rectosigmoid resection had a tendency for less blood loss than open surgery (169 mls, SD 0-3000 vs 238 mls, SD 0-5836) but this was not statistically significant (p = 0.06).

In the MRC-CLASSIC trial, no difference was seen in the transfusion requirements between open and laparoscopic surgery (41 patients [15%] vs 105 patients [20%], respectively; p = 0.11) (Guillou et al 2005). The transfusion requirement rate increased in converted patients (p = 0.01) after adjustment for stratification factors.

Blood loss was less (p = 0.003) in laparoscopic surgery (58mls, range 10-350) than open surgery (mean 137 mls, range 32-355) for resection of T2 and T3 tumours (Hasegawa et

al 2003). Similarly laparoscopic colorectal resection resulted in less blood loss (mean 284 mls, 100-700) compared with open surgery (mean 407 mls, 100-1000; $p < 0.05$) (Curet et al 2000). The highest blood loss was recorded for patients whose operations were converted to open surgery (mean 683 mls, range 100-1200). No laparoscopic patient required a blood transfusion, whereas 2 from the open group and 3 from the converted group required transfusions.

No difference in mean blood loss was found between open surgery (100 mls, range 100-800) and laparoscopic colonic resection (100 mls, range 100-300) in the study from Los Angeles (Kaiser et al 2004). The blood loss was greater in patients whose operation was converted to open surgery (mean 200 mls, range 100-1000). One of the 20 open patients required a blood transfusion (5%) whereas none did in the laparoscopic group. Two patients (15%) in the 13 converted patients received blood.

In the Singaporean RCT of systemic immunity after laparoscopic colectomy for cancer, the authors reported that 15 of all 236 laparoscopic and open surgery patients required peri-operative blood transfusion (6%) (Tang et al 2001). No comparative data were given.

The mean operative blood loss was significantly lower ($p = 0.02$) in laparoscopic TME (20 mls, range 5-120) compared with open TME (92 mls, range 50-200) in the Chengdu RCT (Zhou et al 2004).

In the Sao Paulo RCT of 13 laparoscopic APERs and 15 open APERs, blood transfusion was needed in 3 (23.1%) laparoscopic patients and in 10 (66.6%) open APER patients (Araujo et al 2003). However this difference was not significant (p = 0.46). The number of blood units for the 2 groups was also not significantly different.

In the RCT of resection for benign and malignant colorectal diseases from Milan, the mean operative blood loss was 170 mls (SD 107, median 100, range 50-1600) in 136 laparoscopic operations and 286 mls (SD 242, median 200, range 50-1550) in 133 open resections (p = 0.02) (Braga et al 2002). Twenty-seven (19.8%) patients in the laparoscopic group and 39 (29.3%) patients in the open group received homologous blood transfusion (p = 0.09). In transfused patients, the mean amount of homologous blood given was 439 mls (SD 176) in the laparoscopic group and 487 mls (SD 211) in the open group (p = 0.33).

The same authors report in the same year a smaller cohort of patients in another study of metabolic and functional results after laparoscopic (40 patients) and open (39 patients) surgery for benign and malignant colorectal diseases (Braga et al 2002). Intra-operative blood loss was 123 mls (SD 107) in the laparoscopic group and 319 mls (SD 307) in the open group (p = 0.02). Four patients in each group received peri-operative homologous blood transfusion. In transfused patients, the amount of homologous blood given was 422 mls (SD 176) in the laparoscopic group and 462 mls (SD 211) in the open group (p = 0.89). It is unclear whether this cohort represents a subset of patients from the former study.

Intra-operative blood transfusion was given more frequently ($p < 0.05$) in 30 open operations (median 0 mls, range 0-1200) than in 30 laparoscopic operations (median 0 mls, range 0-0) in the RCT of functional recovery after surgery for benign and malignant colonic conditions (Basse et al 2005). No difference was noted in the requirements for post-operative blood transfusion (open: median 0 mls, range 0-1200; laparoscopic: median 0 mls, range 0-1500).

Comparative, non-randomised studies

The mean estimated blood loss from the Parisian study were 114.9 mls (SD 102.6) for laparoscopic and 265.8 mls (SD 28.8) for open surgery ($p = 0.05$) (Champault et al 2002). Four laparoscopic patients required a median of 3.5 pints (range 2.4) of blood transfusion and seven open patients required a median of 3.7 pints (range 2.5). These differences were not significant.

The median operative blood loss was significantly less ($p = 0.02$) for laparoscopic APER (500 mls, range 100-3000) compared with open APER (1000 mls, range 400-3125) (Leung et al 2000). Similarly, laparoscopic TME resulted in less blood loss (median 250 mls, range 30-3050) compared with open TME (median 1000 mls, range 50-3500; $p < 0.001$) in a case-control study from the Netherlands (Breukink et al 2005). This was particularly the case for laparoscopic low anterior resection (median 175 mls, range 30-2200) compared with open surgery (median 1000 mls, range 50-3200; $p < 0.001$),

whereas blood loss differences in APER did not reach significance (laparoscopic median 475, range 200-3050 vs open median 1600, range 400-3500; $p = 0.11$).

The need for intra-operative blood transfusion was significantly less ($p < 0.001$) in laparoscopic rectal cancer excision (4 out of 101) compared with open procedure (92 out of 334) in the series from Regensburg (Anthuber et al 2003). The estimated blood loss was significantly less ($p < 0.01$) in 18 laparoscopic rectal cancer excisions (mean 136 mls, SD 21) compared with 18 open procedures (mean 357 mls, SD 34) (Wu et al 2003).

Blood loss was significantly less ($p < 0.01$) in patients undergoing laparoscopic colectomy (mean 103 mls, range 10-430) compared with open colectomies (mean 318 mls, range 60-810) (Kakisako et al 2000).

The blood loss in 30 laparoscopic right hemicolectomies was significantly less than in 34 open procedures in the series from Shanghai (mean 112.9 mls, SD 96.3 vs mean 274.5 mls, SD 235.4 respectively; $p = 0.005$) (Zheng et al 2005).

In a prospective case-matched study of patients undergoing laparoscopic ($n = 147$ patients) or open ($n = 147$ patients) colorectal operations for benign and malignant conditions over one year, there was no significant difference in ASA class, body mass index or pre-operative and post-operative haemoglobin levels. However the open colectomy group required significantly more units of blood ($p = 0.003$) to maintain similar haemoglobin levels after surgery. Estimated blood loss ($p < 0.001$) and the

number of patients who received transfusions on the day of surgery (p = 0.002), during the first 48 hours after surgery (p = 0.005) and during the entire hospital stay (p = 0.003) were significantly higher in the open colectomy group (Kiran et al 2004).

Non-comparative studies

In the LCSSG study, the mean blood loss was 412 mls (SD 325) for laparoscopic APERs and 298 mls (SD 250) for laparoscopic anterior resections (Scheidbach et al 2004). The mean intra-operative blood loss for laparoscopic sigmoid resection for cancer was 241 mls (CI 50-500), with 71 (of 292 patients) receiving packed red blood cells peri-operatively in the study from LCSSG (Scheidbach et al 2002).

In the study of 206 laparoscopic left hemicolectomies for cancer from Rennes, no patient received blood intra-operatively (Lechaux et al 2002). Thirteen patients (6%) with 'cardiovascular risk factors' were transfused post-operatively and the mean blood transfusion requirement was 2.2 units of blood (SD 0.4).

In the retrospective New York series of 81 laparoscopic colectomies for cancer, two patients with post-operative bleeding were transfused (4 units and 2 units respectively) with packed red blood cells (Jacob & Salky 2005).

In the study of 120 laparoscopic colectomies versus 31 low anterior resections from Tokyo, the median blood losses were 32 mls (range 5-248) and 60 mls (range 10-265) respectively (p = 0.001) (Yamamoto et al 2004). Two patients out of 194 (1%)

laparoscopic rectal resections for cancer required a blood transfusion in the Berlin series (Bärlehner et al 2005). The median blood loss was 80 mls (range 10-600) in the Hong Kong series of 44 laparoscopic TMEs (Tsang et al 2003). Peri-operative blood transfusion (median 750 mls, range 600-1200) was necessary in 6 out of 32 laparoscopic rectal excisions in the study from Bordeaux (Rullier et al 2003), all of whom were among the first 16 patients to undergo surgery. The mean operative blood loss from a series of 82 laparoscopic TMEs for low rectal cancer was 20 mls (range 5-120) (Zhou et al 2003).

In the German five-centre study that examined 399 patients undergoing laparoscopic colorectal cancer resection, the mean peri-operative transfusion requirement was 0.1 units for sigmoid or left colectomy, 0.6 units for anterior resection, 1.6 units for APER and 0.7 units for right hemicolectomy (Schiedeck et al 2000).

In a series of 50 laparoscopic colonic resections for benign and malignant diseases in elderly or high-risk patients, the median intra-operative blood loss was 50 mls (range 0 - 200) (Bardram et al 2000).

There was no difference ($p = 0.78$) in the blood loss between low volume hospitals (mean 185 mls, median 100 mls), medium volume hospitals (mean 205 mls, median 100 mls) and high volume hospitals (mean 150 mls, median 100 mls) in 536 patients from the COLOR trial (Kuhry et al 2005).

ALSGBI CONCLUSION ON BLOOD LOSS AND THE USE OF BLOOD PRODUCTS:

LAPAROSCOPIC COLORECTAL CANCER SURGERY RESULTS IN LESS BLOOD LOSS AND IN LESS USE OF BLOOD PRODUCTS COMPARED WITH OPEN SURGERY.

9. Incidence of short term complications

Meta-analysis

In a meta-analysis of 12 trials, the differences in peri-operative and early mortality rates were not statistically significant (odds ratio [OR] 0.85, CI 0.33-2.21, p = 0.74, n = 1504) between laparoscopic compared with open colorectal resection. The reduction in the overall morbidity rate (number of patients who had any complication) (OR 0.62, CI 0.45-0.85, p < 0.003, n = 1055) was significant in a fixed effects model but this was no longer the case when a random effects model was used (OR 0.68, CI 0.38-1.24, p = 0.21) (Abraham et al 2004). When data on patients randomised before the operation were analysed separately, there was a minimal change in the magnitude of the effect (OR 0.62, CI 0.44-0.87, p = 0.007, n = 852).

The difference in the total number of complications occurring (excluding re-operation) was statistically significant less in the laparoscopic than open surgery group (OR 0.60, CI 0.45-0.80, p < 0.001, n = 1055). When the random effects model was used, the calculated odds ratio was 0.63 (CI 0.37-1.05, p = 0.06). When only data on patients randomised before operation were analysed, the change in the magnitude of the effect was minimal (OR 0.60, CI 0.44-0.82, p < 0.001, n = 852).

The main difference was less local complications in laparoscopic than open surgery (OR 0.51, CI 0.36-0.73, p < 0.001). This was most obvious in the case of wound infection rates (OR 0.47, CI 0.28-0.80, p = 0.005, n = 1055).

The risk of respiratory complications were lower in the laparoscopic resection than open surgery but statistical significance was not reached (OR 0.65, CI 0.28-1.49, p = 0.30). Similarly there were less re-operations in laparoscopic than open but this was not significant (OR 0.70, CI 0.34-1.46, p = 0.34). The differences between the two groups in terms of total anastomotic leakage rates (overt and contained) were in favour of laparoscopic surgery but differences were small and not statistically significant (OR 0.84, CI 0.45-1.57, p = 0.58). Similar results were obtained for cardiac complications (OR 0.81, CI 0.36-1.81, p = 0.60), deep venous thrombosis (OR 0.81, CI 0.25-2.61, p = 0.72) and other systemic complications (OR 0.95, CI 0.59-1.52, p = 0.82).

Comparative, randomised studies

In the trial from Barcelona, one patient from the laparoscopic group and three from the open group died within 30 days of surgery (relative risk of peri-operative mortality 0.49, CI 0.09-2.68). The overall morbidity was significantly lower in patients who underwent laparoscopic colectomy than open surgery (relative risk 0.49, CI 0.30-0.82) (Lacy et al 2002). Particularly of note were the lower incidences of wound infection (laparoscopic: 8 out of 111 patients vs open: 18 out of 108 patients) and persistent ileus (laparoscopic: 3 out of 111 patients vs open: 9 out of 108 patients).

In the COST study, there were no significant differences between laparoscopic and open colectomy in the rates of intra-operative complications (laparoscopic: 4% vs open: 2%, p = 0.10), 30-day post-operative mortality (p = 0.40), rates and severity of post-operative

complications at discharge (p = 0.98) and at 60 days (p = 0.73), and rates of re-admission (12% and 10%, respectively; p = 0.27), or the rates of re-operation (<2% in each group, p = 1.0) (The COST study group 2004). Intra-operative complications included splenic injury (2 in the open-colectomy group), bleeding (1 in the open-colectomy group and 8 in the laparoscopic-surgery group), bowel injury (2 and 6, respectively), and miscellaneous (3 and 2, respectively).

Operative mortality (30-day) was not significantly different between laparoscopic (0.6%) and open (2.4%) rectosigmoid resection (Leung et al 2004). Furthermore there was no difference between the overall morbidity rate between laparoscopic (40 out of 203 patients) and open (45 out of 200 patients) surgery. There were 9 wound infections in the laparoscopic group and 15 in the open group. Re-operation was necessary in 6 laparoscopic patients and in 5 open surgery patients.

In the MRC-CLASSIC trial, 34 patients died in hospital (13 [5%] after open surgery vs 21 [4%] after laparoscopic surgery; difference -0.9%, CI -3.9 to 2.2%, p = 0.57) (Guillou et al 2005). Patients who underwent conversion had a higher death rate than open or laparoscopic patients (13 [9%] vs 15 [5%] and 16 [1%], respectively). However, this difference was not significant after adjustment for stratification factors (p = 0.34). The main cause of death was cardiorespiratory failure (16, 47%). 81 (10%) patients had intra-operative complications, with no difference between laparoscopic and open colorectal resection (difference 0.2%, CI -4.2 to 4.6%, p = 0.93). Clinically significant intra-operative haemorrhage and cardiac insufficiency/dysrhythmia were the most common

complications. Complication rates were higher for rectal than colon procedures (51[13%] of 381 vs 30 [7%] of 413, respectively). The rate was also higher in converted than in non-converted patients and in those who underwent open surgery, even after adjustment for stratification factors ($p = 0.002$).

257 (32%) patients had 30-day post-operative complications in the MRC-CLASSIC trial. No difference was recorded between treatments (difference 1%, CI -5.9 to 7.8%, $p = 0.78$). Chest infection was more common in laparoscopic than open surgery (43 [8%] vs 10 [4%]), of which most were pneumonias. 18 (42%) of 43 respiratory infections in the laparoscopic arm were in converted patients. Complication rates between actual treatment groups did not differ after adjustment for stratification factors ($p = 0.04$). Again, rates were higher for rectal than for colonic procedures (148 [39%] vs 109 [26%]). 56 (7%) patients had 3-month post-operative complications, which also did not differ between treatments (difference -0.1%, CI -3.8 to 3.7%, $p = 0.98$). Intestinal obstruction and persistent wound infection were the most frequent complications. Similar rates of major or minor complications were recorded for both treatment groups (41 [5%] major, 27 [3%] minor). Complication rates at 3-month follow-up did not differ for converted patients ($p = 0.35$).

In the economic comparison of 98 laparoscopic and 112 open colonic resections in the COLOR trial, there were no peri-operative deaths in either group during first admission but one in the laparoscopic group after discharge. There was no difference in the complication rates during the first admission (laparoscopic 21% vs open 16.1%) and after

discharge (laparoscopic 12% vs open 7.1%) (Janson et al 2004). However re-operations were more frequent in the laparoscopic group during the first admission (laparoscopic: 8 vs open: 4) and after discharge (laparoscopic: 6 vs open: 3). However these differences were not tested for statistical significance owing to the small number of observations. After discharge, 12 patients (of 98) in the laparoscopic group and 8 patients (of 112) in the open group developed complications. Re-operations were required in 6 and 3 patients respectively.

In an RCT of 83 patients undergoing laparoscopic or open colectomy from St. Louis, 46 open surgery patients had a significantly higher rate of ileus compared with 37 patients who had laparoscopic resection (30.4% vs 5.4%, respectively; $p = 0.004$) (Winslow et al 2002). Post-operative pulmonary complications were similar between groups (open 6.5% vs laparoscopic 5.4%), and no patient in either group developed post-operative urinary retention. Wound infections occurred in 10.9% ($n = 5$) of patients in the open colectomy group compared with 13.5% ($n = 5$) of the laparoscopic-treated patients (not significant). Of the 5 wound infections in the laparoscopic group, only 1 was at the trocar site; the other 4 were extraction site infections. The incidence of wound infection in the extraction site incisions (10.8%) was identical to that in the open incisions (10.9%). In the laparoscopic group, wound infections occurred in 27% of suprapubic extraction sites versus only 3% of umbilical extraction sites (not significant). Although it appeared that the suprapubic sites were more frequently infected, the number of wound infections at either site was too small to draw any reasonable conclusions.

In the RCT study of immunity of 118 laparoscopic and 118 open resections for cancer from Singapore, 27 (16 laparoscopic, 11 open) experienced intra-operative complications and 13 (8 laparoscopic, 5 open) had post-operative complications (Tang et al 2001). The main intra-operative complication was significant haemorrhage requiring peri-operative blood transfusion in 15 patients (6%). Six post-operative wound infections were noted, 3 occurring in each treatment group. Two anastomotic leaks occurred in the laparoscopic group compared with one in the open group.

The peri-operative morbidity was significantly higher ($p = 0.01$) in 89 open TMEs (12.4%) than in 82 laparoscopic TMEs (6.1%) from the Chengdu study (Zhou et al 2004). There were more urinary retentions (open: 4, laparoscopic: 2), post-operative infections (open: 3, laparoscopic: 2) and anastomotic leaks (open: 3, laparoscopic 1).

No significant difference ($p = 0.22$) was noted in total complication rates between 24 laparoscopic (1 patient) and 26 open resections (5 patients) for T2 or T3 colorectal cancers (Hasegawa et al 2003). No deaths were recorded in either group.

In the study from New Mexico, one out of 25 patients required conversion to open laparotomy because of extensive disease (Curet et al 2000). She developed ischaemic bowel from tumour involvement of the mesentery and died of sepsis 6 weeks post-operatively. No other peri-operative deaths occurred in either open or laparoscopic colectomy. One minor and one major complication occurred in the laparoscopic group. In

the open group, 3 patients had 5 complications, 4 of which were major. Wound problems were similar in both groups.

There were no peri-operative complications or death in the RCT from Los Angeles (Kaiser et al 2004). Post-operatively, one major (congestive heart failure; 5%) and three minor complications (two with prolonged ileus [10%], one with lung atelectasis [5%]) occurred in the open group, whereas one patient developed a urinary tract infection (7%) in the laparoscopic group. Three patients in the converted group developed lung atelectasis (23%) and one had prolonged ileus (8%).

In the Sao Paulo RCT of 13 laparoscopic APERs and 15 open APERs, post-operative complications were observed in 9 (69%) patients in the former group and in 7 (46.7%) in the latter group (Araujo et al 2003). There was no significant difference between these rates. In the laparoscopic group, there were 4 perineal wound dehiscences, 2 perineal hernias, 1 urinary retention, 1 chest infection and 1 delayed recovery of bowel function. In the open group there were 3 perineal wound dehiscences, 3 delayed recoveries of bowel function and 1 urinary retention.

In the Milanese RCT of 136 laparoscopic versus 133 open colorectal operations for benign and malignant diseases, one patient (laparoscopic) died in the post-operative period of massive upper gastrointestinal bleeding (Braga et al 2002). The overall morbidity rate was 20.6% (CI 13.8-27.4%) in the laparoscopic group versus 38.3% (CI 34.1-42.5%) in the open group ($p = 0.003$). Fewer patients had infectious complications

in the laparoscopic group (11.0%; CI 5.7-16.3%) compared with the open group (23.3%; CI 16.1-30.5%). The difference in the infection rate between the two groups (12.3%; CI 3.7-21.2%) was significant (p = 0.01). Re-operation was necessary in 8 (5.9%) patients in the laparoscopic group (6 anastomotic leaks, 1 adhesions, 1 bowel herniation through a 12 mm trocar site) and in 13 (9.8%) patients in the open group (8 anastomotic leaks, 3 adhesions, 2 bleeding) (p = 0.34). The laparoscopic group has a lower wound infection rate (5.9%, CI 1.9-9.9%) than the open group (15.0%, CI 8.9-21.1%; p = 0.02). No significant differences (p = 0.20) were noted in non-infectious complications between laparoscopic (7.3%) and open (12.8%) procedures. Anastomotic leak rate was also not significantly different (p = 0.59) between laparoscopic (5.9%) and open (8.3%) surgery.

The same authors report a smaller RCT examining metabolic and functional results after laparoscopic surgery for benign and malignant colorectal diseases (Braga et al 2002). No peri-operative deaths occurred and the overall morbidity rate was 26.6% (21/79 patients). In the laparoscopic group, the morbidity rate was 20.0% (8/40 patients) vs 33.3% (13/39 patients) in the open group (p = 0.28). Post-operative infections occurred in 3 laparoscopic patients (7.5%) and in 10 patients (25.6%) who underwent open surgery (p = 0.06). Anastomotic leak rate was 2.5% (1/40 patients) in the laparoscopic group and 7.7% (3/39 patients) in the open group (p = 0.30). It is unclear whether this cohort represents a subset of patients from the former study.

In an RCT examining functional recovery after 30 laparoscopic and 30 open colonic resections for benign and malignant conditions, post-operative complications were seen

in 6 patients in the open group and 8 patients in the laparoscopic group (Basse et al 2005). 4 patients developed wound infection in the laparoscopic group compared with 1 in the open group. Two patients developed wound dehiscence and two had cardiopulmonary complications in the open group. Three patients died in the open group, 2 of cardiopulmonary causes on days 1 & 2, and 1 was re-operated for anastomotic leakage on day 8 and died at day 19 after a third operation for wound dehiscence on day 12. Eight patients in the open group and 6 patients in the laparoscopic group were readmitted after discharge.

Comparative, non-randomised studies

Mortality and morbidity rates were not significantly different between laparoscopic and open resection in the study from Orlando (Patankar et al 2003). Two of the 172 (1.2%) laparoscopic patients died compared with four (2.4%) in the open group ($p = 0.45$). 18 laparoscopic patients (10.4%) had early complications compared with 12 (7%) in the open group ($p = 0.25$). Five laparoscopic patients developed ileus and three bled post-operatively whereas none in the open group had these problems.

No deaths occurred in either laparoscopic or open colorectal resection in the Parisian study (Champault et al 2002). The overall morbidity was significantly lower among patients treated with laparoscopy than among those who had open surgery (13.5% vs 33.7%, $p = 0.001$). Prolonged ileus of more than 4 days ($p = 0.01$) and intra-abdominal abscess ($p = 0.05$) were significantly more frequent in the open than laparoscopic surgery group.

In the study from Candiolo, the in-hospital mortality rate was 0.08% (Capussotti et al 2004). Two patients, both in the open surgery group, died in the post-operative period from pulmonary embolism. Overall, in-hospital morbidity was 14.1%: 16.2% in the laparoscopic and 13.3% in the open group (p = 0.56). The anastomotic leakage rate was 7.6% in both groups. Re-operation rates were 10.8% in the laparoscopic and 8.8% in the open group.

Three patients (5.7%) died in the laparoscopic right hemicolectomy compared with 1 (2.3%) in the open surgery group (p = 0.77) in the study from Rome/Ancona (Lezoche et al 2002). No operative deaths occurred in the laparoscopic left hemicolectomy group, but one (1.6%) died in the open left hemicolectomy group (p = 0.91). There were no significant differences in major complication rates between laparoscopic (1.9%) and open (2.3%) right hemicolectomies (p = 0.56). Similarly the morbidity rates were not significantly different between laparoscopic (7.5%) and open (6.3%) left hemicolectomies (p = 0.94). In their follow-up series by the same authors, mortality was observed in 2 high risk patients (ASA IV) and 1 ASA III patient in the laparoscopic right hemicolectomy group (2.7%), as well as in 1 ASA IV patient in the open group (1.7%; p = 0.90) (Lezoche et al 2003). No operative mortality occurred in the laparoscopic left hemicolectomy group, while 1 ASA III patient in the open group (0.9%) died in the post-operative course (p = 0.74). In the laparoscopic right hemicolectomy group, 2 patients (1.8%) underwent re-operation for anastomotic leak and ileus compared with the open group whose overall morbidity rate was 1.7% (1 haemoperitoneum; p = 0.30). In the left

hemicolectomy series, morbidity was higher in the open group (laparoscopic 4.1% [2 leaks, 3 enteric fistulas, 1 haemoperitoneum, 1 ileus, 1 ischaemic colitis] vs open 4.9% [2 leaks, 1 enteric fistula, 1 haemoperitoneum, 1 ileus). The differences, however, were not statistically significant ($p = 0.99$).

Two post-operative deaths from myocardial infarction were reported from a group of 61 patients who underwent laparoscopic resection (Hartley et al 2000). No deaths were reported for the open surgery group and morbidity data were not presented in this series. The early post-operative mortality was two deaths in 61 open APERs compared with one in 28 laparoscopic APERs (this patient was converted to open surgery) (Baker et al 2002). Again no morbidity data were reported in this study.

No operative mortality was recorded for 25 laparoscopic and 34 open APERs from the Hong Kong study (Leung et al 2000). 22 complications arising in 12 laparoscopic patients and 39 complications in 21 open patients were noted. Primary healing failure of the perineal wound and urinary tract problems were common in both groups. In 24 patients (96%) of the laparoscopic group and 26 (76.5%) of the open group, the perineal wounds healed completely on first follow-up ($p = 0.08$).

In a Dutch study of laparoscopic 41 TMEs compared with 41 historical open TMEs, there was one death (pulmonary embolism and mesenteric thrombosis 14 days post-operatively) in the open group (2%) and none in the laparoscopic group (Breukink et al 2005). The overall morbidity rate was 51% (21 out of 41) for the open group and 37%

(15 out of 41) for the laparoscopic group ($p = 0.26$). No differences were found between low anterior resection and APER in the laparoscopic group ($p > 0.05$). Leaks were found in two out of 23 anastomoses (9%) in the laparoscopic group compared with four out of 28 anastomoses (14%) in the open group. There were more cardiopulmonary complications and urinary tract infections in the open group (8 and 6 respectively, out of 41) compared with the laparoscopic group (5 and 3 respectively, out of 41). Wound healing problems were also more common in the open group (2 wound infections, 2 perineal wound infections and 1 fascial dehiscence; total 12%) than in the laparoscopic group (2 perineal wound infections; total 5%). Re-intervention was also more frequent in the open group (2 for anastomotic leaks, 1 for bleeding, 2 for intra-abdominal abscess drainage, 1 radiological drainage of abscess, 1 for small bowel perforation and 1 for mesenteric thrombosis; total 20%) than the laparoscopic group (2 for anastomotic leaks, 2 for bleeding, 1 for ileus; total 12%).

In the case-control series of 144 laparoscopic TMEs from Bordeaux/Marseille, the post-operative mortality was 1% (one patient presented with colonic ischaemia and died from septicaemia) (Bretagnol et al 2005). Post-operative morbidity occurred in 50 patients (34%) and included 33 cases of pelvic sepsis (anastomotic leakage or pelvic abscess). No comparative data were presented for the open TMEs.

There were less surgical complications ($p = 0.003$) in laparoscopic rectal cancer excision (11 out of 101) compared with open surgery (83 out of 334) in the series from Regensburg (Anthuber et al 2003). Similarly general complication rates were also

significantly less (laparoscopic 20 out of 101, open 134 out of 334; $p < 0.001$). The anastomotic leak rate was similar between the two groups (laparoscopic 9, open 25; $p = 0.73$). Five deaths occurred in the open group compared with none in the laparoscopic group ($p = 0.17$).

One operative death was noted in 32 laparoscopic rectal excisions from Bordeaux compared with none in 43 historical open procedures ($p = 0.42$) (Rullier et al 2003). Major surgical morbidity was observed more frequently after laparoscopy (10 out of 32 patients) than laparotomy (5 out of 43 patients), although the difference was not significant ($p = 0.34$). The death in the laparoscopic group was due to septicaemia following rectal excision after re-operation for distal colonic ischaemia. The laparoscopic complications were colonic ischaemia (2 patients), coloplasty pouch fistula with abscess (3), rectovaginal fistula (1), isolated pelvic abscess (1), obstruction (2) and ileostomy ischaemia (1). No coloanal anastomotic leakage occurred. Short-term urinary retention occurred in 4 laparoscopic patients.

Post-operative complications were more frequent in 18 open rectal cancer excisions than in 18 laparoscopic procedures from Nanjing (27.8% vs 5.6%, respectively; $p < 0.05$) (Wu et al 2003). No anastomotic leak occurred in this series.

There were no statistical difference ($p = 0.83$) in the proportion of patients who experienced a major complication between laparoscopic (15 out of 98 patients) and open (32 out of 219 patients) colorectal resection from Hamilton (Hong et al 2001). Most

complications were cardiac-related (laparoscopic: 10 out of 15 patients vs open 16 out of 32 patients). One wound dehiscence in the laparoscopic group occurred in patient who was converted to the open procedure. There were four anastomotic leaks in the open group and none in the laparoscopic group. There was a greater proportion of patients who experienced minor complications in the open technique (laparoscopic:11 patients vs open: 47 patients, $p = 0.02$). Nineteen patients (out of 219) developed wound infections in the open group whereas there were only 4 in the 98 laparoscopic patients. Fourteen patients developed ileus in the open group whilst there were 5 in the laparoscopic group. Eight patients had basal atelectasis in the open group but none occurred in the laparoscopic patients. There were 8 urinary infections in the open group and one in the laparoscopic patients. Three of the 11 patients who experienced a minor complication were patients who were converted to the open technique (2 with ileus and 1 with wound infection). There was no difference in peri-operative mortality between the two groups. Four deaths (1.8%) occurred in the open group (3 myocardial infarctions and 1 sepsis) and three deaths (3.1) occurred in the laparoscopic group (3 myocardial infarctions).

Three deaths were reported amongst ninety nine patients in the early post-operative period from the study of laparoscopic right hemicolectomy in Hull (Baker et al 2004). Two occurred in the 66 open patients and one in the 33 laparoscopic patients. Two of the deaths were a consequence of pneumonia (one in each of the groups) and the second death in the open group followed sepsis secondary to an anastomotic leak. There were 19 post-operative complications (19.2%), 5 (15.1%) in the laparoscopic group and 14 (21.2%) in the open group. There were 5 anastomotic leaks (3 in the open cohort and 2 in

the laparoscopic). Of the 2 patients who had haemorrhage in the open group, one was treated conservatively and the other required re-laparotomy and over-sewing of an oozing mesenteric edge. Although there seemed to be trend toward an increase in septic complications in the open cohort, this did not reach statistical significance.

Five out of 30 patients (16.7%) who underwent laparoscopic right hemicolectomy for cancer from Shanghai developed post-operative complications (Zheng et al 2005). Two had pulmonary infections, two had wound infections and one developed incomplete intestinal obstruction. The morbidity in the open group (10 out of 34 patients [29.4%]: 3 pulmonary infections, 4 wound infections, 1 urinary tract infection, 1 anastomotic leak and 1 massive haemorrhage) was slightly higher than in the laparoscopic group but the difference was not statistically significant ($p = 0.23$).

In the Miami series, complications occurred in 23 patients (23%) in the early post-operative period (Lujan et al 2002). Three patients with early small bowel obstruction responded to conservative measures and did not require re-operation. One patient died post-operatively because of cardiac complications (mortality < 1%). No comparative data with open surgery were presented.

No patient in the laparoscopic group for Dukes' A cancers (20 patients) experienced serious complications during or after surgery, although 3 elderly patients had delirium, 2 had wound infections and one had adhesive ileus (Kakisako et al 2000). No comparative data were presented for open surgery from this series.

In the Singapore series of laparoscopic surgery for benign and malignant colorectal diseases, there was no overall difference ($p = 0.35$) in the general complication rates between laparoscopic (6 out of 35 patients) and open (9 out of 42 patients) (Koh et al 2005). Four out of 7 converted patients had general complications. There were no respiratory complications in the laparoscopic group. Furthermore there were no complications related to the wound (infection or dehiscence) in this group, compared with 4 out of 42 open patients ($p < 0.001$) and 2 out of 7 converted patients.

In a series of 338 laparoscopic colorectal resections for benign and malignant diseases, the converted group had a wound infection rate of 7.5%, which was 4% higher than the laparoscopic group (Gibson et al 2000).

In a blinded prospective study of the incidence of deep venous thrombosis (DVT) following open or laparoscopic colorectal resections, post-operative duplex ultrasonography revealed 3 DVTs (6%) in the posterior group of calf veins after open sigmoid resection but none in the laparoscopic group (Mall et al 2001). The post-operative recovery of patients with a DVT was uneventful; repeat duplex imaging before discharge from hospital showed no sign of ascending thrombosis or floating thrombus in the leg veins. The maximum risk of a DVT occurring in the laparoscopic group ($n = 32$) after laparoscopic colorectal resection was estimated to be 9% (CI 0-9%).

Non-comparative studies

In the LCSSG study, the mortality rate was 2% (3 patients) in the 149 laparoscopic APER patients (Scheidbach et al 2002). Overall, 117 complications and post-operative problems were observed in 55 patients, representing a morbidity rate of 36.4% Re-operation necessitated by complications, however, was observed in only 8 patients (5.4%). The mortality rate was 1.2% (3 patients) in the 231 laparoscopic anterior resection patients. 88 patients (38.1%) developed complications in whom 20 required re-operations (8.6%). Overall, 32 cases of anastomotic leaks were recorded (13.8%). The anastomotic insufficiency rate increased with decreasing distance of the rectal lesion from the anal verge. No significant differences in morbidity and mortality were noted between the two laparoscopic groups. In their follow-up study, the mortality rate was 1.6% (3 of 190 patients) in laparoscopic APER and 1.5% (5 of 330 patients) in laparoscopic anterior resection (Scheidbach et al 2004). Intra-operative complication rates were similar for both groups (5.4%). Re-operation rates were 5.3% for laparoscopic APER and 8.1% for laparoscopic anterior resection. Overall morbidity rate was 33.2% (63 of 190) in laparoscopic APER and 33.3% (110 of 330) in laparoscopic anterior resection. Overall anastomotic leak rate was 4.8% (16 of 330) in the latter group, increasing significantly the closer it is to the anal verge (less than 10 cm from anal verge, leak rate 16.8%; more than 10 cm from anal verge, leak rate 8.2%, $p = 0.03$).

The same study group reported a mortality rate of 2.7% for laparoscopic sigmoid resection for cancers (8 out of 292 patients) (Scheidbach et al 2002). Cause of death was peritonitis resulting from a surgical complication in 4 patients, and general medical

complications in 4 patients (3 with cardiopulmonary complications and 1 with cerebrovascular event). Post-operative complications occurred in 65 patients, representing a morbidity rate of 22.3%. The major surgical complications were 3 post-operative haemorrhages necessitating re-operation (1%), 8 patients (2.7%) with transit disorders of more than 3 days duration including one case of obstruction requiring surgical treatment, and 9 confirmed anastomotic insufficiencies (3%). Re-operation was necessary in a total of 9 patients (3%).

Two peri-operative deaths were reported from the series of 181 patients who underwent laparoscopic colorectal surgery in Brisbane (Lumley et al 2002). One was tumour-related after a palliative Hartmann's procedure. The other occurred after a second-look laparoscopy for failure to improve after right hemicolectomy. At this second procedure the small bowel was inadvertently perforated, and the patient developed necrotizing fasciitis. Six patients experienced post-operative intestinal obstruction (3%). One of these occurred in a patient with APER conversion and the other five after laparoscopic anterior resections. Five of the six patients required surgery for their obstructions.

In the series of 102 laparoscopic TMEs for rectal cancer, the overall 30-day mortality rate was 2% (Leroy et al 2004). One patient with extensive coronary artery disease and known left ventricular dysfunction died of septic shock secondary to an anastomotic leak; the other was due to multi-organ failure in the setting of a post-operative bleed. The overall post-operative morbidity was 27%. The total anastomotic leak rate was 17%: 11% were clinical leaks and 6% were revealed solely on contrast radiography, which was

performed as a routine post-operative examination. Five patients developed urinary retention and only one patient had a wound infection.

Post-operative complications developed in 58 patients (26.3%) out of 220 patients who underwent laparoscopic rectal excisions for cancer in Barcelona (Delgado et al 2004). 10.4% (23 patients) of them were major complications and 15.9% (35 patients) were minor complications. The rate of suture dehiscence was 7.3% (12 of 163 patients in whom sphincter preservation was undertaken). In all cases, this complication was resolved with conservative measures and the use of laparoscopic techniques. The post-operative mortality rate (first 30 days after surgery) was 1.3%.

No post-operative mortality was noted in a series of 194 laparoscopic rectal cancer resections from Berlin (Bärlehner et al 2005). There were 39 post-operative complications (20.1%) and the most common was anastomotic leak (13.5%). The frequency of other complications such as bleeding (1%), rectovaginal fistula (1.6%), ileus (1.6%) and wound infections (1.6%) was low. Re-laparoscopy was necessary in 5.1% of the patients and a laparotomy in 6.2%.

No peri-operative deaths occurred in 44 patients with mid or low rectal cancer who underwent laparoscopic TME with construction of a colonic J pouch (Tsang et al 2003). Fifteen patients developed 17 early complications (11 transient urinary retention, 2 ileostomy complications, 1 port-site hernia, 1 urinary tract infection, 1 wound infection and 1 adhesive obstruction). Re-operations were required for three patients (2 ileostomy

complications, 1 port-site hernia). In 4 patients who were asymptomatic, minor radiological leakage was detected after hospital discharge by routine contrast enema.

There were three complications (2 urinary retentions and 1 anastomotic leakage) from a series of 82 patients who underwent laparoscopic TME for low rectal cancer with anal sphincter preservation from Chengdu (Zhou et al 2003). No mortality was reported.

In a series of 80 laparoscopic TMEs for rectal cancer (52 anterior resections and 28 APERs), the overall wound infection rate was 8.7% (7 out of 80), resulting mainly from perineal infections after APERs (5 out of 7) (Poulin et al 2002). Pneumonia developed in 3 patients (3.7%). Although 14 patients (17.5%) presented with urinary retention requiring re-insertion of the urinary catheter, urinary tract infection developed in only one (1.2%). No patient had intra-abdominal sepsis or abscess. After anterior resection, the anastomotic leak rate was 5.7% (3 out of 52).

In 50 laparoscopic operations for stage III colon cancer, an operative mortality of 2% (one patient with massive stroke) was reported (Franklin et al 2000). One anastomotic leak developed after a left hemicolectomy, requiring re-operation for faecal diversion. One patients developed perineal wound infection after APER.

In the series of 206 laparoscopic left hemicolectomies for cancer, two patients died post-operatively within 30 days (undiagnosed cerebral metastasis and pulmonary embolism) (Lechaux et al 2002). Post-operatively complications occurred in 24 patients (11%).

Clinical anastomotic leaks developed in 5 patients (2.4%) and there were also 5 wound infections (2.4%). Four patients developed bowel obstruction and the overall rate of re-intervention was 3% (four for anastomotic leaks and two for obstruction). Four patients (2%) developed urinary retention (> 2 months) and four patients developed medical complications (2%).

In laparoscopic surgery for stage I colorectal cancer, no peri-operative deaths were reported in 130 patients (Watanabe et al 2003). Post-operative complications occurred in 19 patients (14.6%), including wound sepsis in eight patients (6.2%), anastomotic leaks in four (3.1%), and bowel obstruction in three (2.3%). None of the patients required re-operation for bowel obstruction. Of the four patients who developed anastomotic leakage, three had undergone anterior resection for rectal cancer.

Overall, a total of 15 early and late post-operative complications were observed in 13 patients out of 70 (18.6%) who underwent laparoscopic rectosigmoid and rectal resections (Yamamoto et al 2002). There was no laparoscopic-related cardiopulmonary morbidity. Re-operation was required in 6 patients (8.6%): 2 with anastomotic leaks and 1 with a post-operative rectovaginal fistula who underwent stoma creation; 1 patient underwent laparoscopic re-operation for repair of an unrecognised enterotomy; another underwent laparoscopic division of an adhesive band for a post-operative small bowel obstruction; and 1 patient developed necrosis of the proximal colon that required laparotomy (with resection of the colon and re-anastomosis). There were no significant

differences in complication rates between patients with rectosigmoid/upper rectal cancers and those with lesions in the middle/lower rectum.

One post-operative death from anastomotic leak was noted in a series of 81 patients (1.2%) who underwent laparoscopic colectomy for cancer from New York (Jacob and Salky 2005). The overall 30-day peri-operative morbidity rate was 13.6% and included wound infection (n = 3), urinary tract infection (n = 2), endoluminally bleeding staple line (n = 2), partial small bowel obstruction (n = 2), pneumonia (n = 1), and deep venous thrombosis (n = 1).

One post-operative death was reported in a series of 56 patients who underwent laparoscopic right hemicolectomy for cancer in Croatia (Baća et al 2005). 10 complications were recorded (3 haemorrhages, 3 wound infections, 2 ileus, 2 anastomotic insufficiencies) and 2 patients required surgical re-intervention.

No peri-operative mortality was reported in 120 laparoscopic colectomies and 31 laparoscopic low anterior resections for cancer in a study from Tokyo (Yamamoto et al 2004). Sixteen patients (13.3%) experienced 17 complications in the colectomy group whereas 5 laparoscopic patients (16.1%) had complications (p = 0.77). The most common complications were wound sepsis (colectomy 4, anterior resection 2), bowel obstruction (colectomy 6, anterior resection 1) and urinary tract infection (colectomy 3, anterior resection 0). No anastomotic leak occurred in this study. No significant differences in complication rates were observed between the two groups.

In the German five-centre study that examined 399 patients undergoing laparoscopic colorectal cancer resection, the 30-day mortality rate was 2% for sigmoid or left colectomy and 2% for APER with no other deaths reported (total 7 deaths, overall 30-day mortality rate 1.8%). Causes of death were anastomotic leakage (n = 5), haemorrhage (n = 1), and septic shock (n = 1). The total complication rate was 27.3% for sigmoid or left colectomy, 26.4% for anterior resection, 44.2% for APER and 11% for right hemicolectomy, giving an overall complication rate of 36.6% (Schiedeck et al 2000). Complications requiring further operation was 8.1% for sigmoid or left colectomy, 6.4% for anterior resection, 15.7% for APER and 5% for right hemicolectomy. Complications treated conservatively was 19.2% for sigmoid or left colectomy, 20% for anterior resection, 28.5% for APER and 6% for right hemicolectomy.

In the Turin study of 108 patients who underwent laparoscopic colorectal resection for benign and malignant conditions, no peri-operative deaths were reported (Degiuli et al 2004). Intra-operative complications were observed in 2 patients (2.1%). Both patients developed intra-abdominal haemorrhage, one of whom required conversion to open surgery. The overall rate of post-operative complications was 11.9%. Early post-operative complications were seen in 6 patients (5.5%). Two of them, abdominal bleeding and bowel obstruction, were major complications, that required further surgery during the post-operative course. There were no anastomotic leaks. The morbidity rate was higher after low anterior resections (16.4%) than after the other left colectomies. No complications were observed after right colectomy. The incidence of complications was

not related to the diagnosis. However it decreased from 17.1% in the first 35 patients, to 14.3% in the second 35 patients, and to 5.2% in the last 38 patients treated.

In the series of 154 benign and malignant rectal neoplasms undergoing laparoscopic TME, the 30-day mortality rate was 2%: one case of intestinal infarction in an elderly patients on post-operative day 4, and one myocardial infarction on post-operative day 2 (Morino et al 2003). The overall post-operative morbidity was 36% (36 out of 100 patients). Complications related to clinically diagnosed anastomotic leakage occurred in 17 patients and were treated in 9 cases with diverting stomas, in 6 cases with surgical or radiological drainage, and in 2 patients with prolonged total parenteral nutrition. There were three cases of prolonged post-operative ileus, treated medically in 2 cases and surgically in 1 case. There were 4 infections of the mini-laparotomy incision site. No general complications such as pulmonary or cardiac were observed if the case of fatal myocardial infarction is excluded. A total of 10 re-operations were performed: 9 stomas to treat fistulas and one intestinal resection in a case of prolonged post-operative bowel obstruction.

In a series of 181 laparoscopic sigmoid colectomies for benign and malignant conditions, anastomotic leaks occurred in 2 patients (1.1%), one of whom died of multiorgan failure, yielding an operative mortality of 0.6% (Senagore et al 2003). The overall complication rate was 6.6% and included 2 patients with ileus, one urinary tract infection, one anastomotic haemorrhage (managed non-operatively), one mesenteric venous thrombosis, two patients with chest pain treated with nitrates, and two episodes of atrial fibrillation

managed medically. The 30-day readmission rate was 7.7% (14 out of 181), the reasons for which include 2 anastomotic leaks (1.1%), 2 pelvic abscesses requiring percutaneous drainage (1.1%), 8 small bowel obstructions not requiring surgery (4.47%), 1 small bowel obstruction requiring surgery (0.6%) and 1 mesenteric venous thrombosis (0.6%).

Post-operative complications were recorded in 8 out of 50 elderly or high-risk patients undergoing laparoscopic colonic resection for benign and malignant conditions (Bardram et al 2000). Two developed anastomotic leaks and three developed mechanical bowel obstruction. Among the patients with complications, 2 had been discharged on days 2 and 3. One patient was readmitted with signs of small bowel obstruction on day 5 and underwent re-operation on day 9; the other patient was re-admitted on day 9 with abdominal pain and had re-operation for anastomotic leakage. No other patients were re-admitted and two deaths were recorded.

No deaths were reported in 17 octogenarians who underwent laparoscopic colonic surgery for benign and malignant diseases (Yamamoto et al 2003). The morbidity rate was 11.8% (2 out of 17) compared with 20.6% (7 out of 34) in the group of patients less than 60 years old who underwent laparoscopic colonic surgery ($p = 0.69$). In the octogenarians, there was one wound sepsis and one abscess. Wound sepsis was more common in the young group (6 patients; $p = 0.40$) and there were also one anastomotic leak and one haemorrhage in this group.

The LCSSG reported a 30-day mortality rate of 1.3% (63 of 4834 patients) in those undergoing laparoscopic surgery for benign and malignant colorectal diseases (Rose et al 2004). The main causes of death were cardiac disease, septic complications following an anastomotic leak (11 patients), pneumonia (8 patients), and progression of the underlying malignancy (8 patients). The overall morbidity rate was 20.1% - 969 patients developed a total of 1379 complications, the most common being urinary tract infection (4.9%), wound healing disorders (4.8%), anastomotic leak (3.1%), ileus (4.5%) and cardiopulmonary problems (4.0%). Re-operations due to haemorrhage (1.6%), anastomotic leak or ileus became necessary in 202 patients (4.2%).

In a Brazilian series of 1966 laparoscopic surgery for benign (59.5%) and malignant (40.5%) colorectal diseases, postal questionnaire survey revealed a post-operative mortality rate of 1.5% (29 patients, range 0-3.2) (Campos et al 2003). The most common causes of death were sepsis (8 patients, 0.4%), respiratory problems (5 patients, 0.3%), anastomotic fistulae (4 patients, 0.2%), cardiac arrhythmia (3 patients, 0.2%), coagulation disturbance (3 patients, 0.2%) and heart attack (3 patients, 0.2%). There was one case each of intestinal obstruction, intestinal lesion and bleeding causing death. The intra-operative complication rate was 4.2% (82 patients, range 2-9.8) and the post-operative complication rate was 19.6% (385 patients, range 8-29.6). The commonest cause of post-operative complications were wound infections (106 patients, 5.4%), anastomotic fistulae (55 patients, 2.8%), coagulation disturbances (28 patients, 1.4%), abdominal abscesses (23 patients, 1.2%), incisional herniae (21 patients, 1.1%) and intestinal obstructions (19

patients, 1.0%). Complication rates were higher in the early phase of experience (first 50 cases) compared with later (25.1% vs 16.1% respectively).

In a series of 150 laparoscopic colorectal procedures for benign and malignant diseases, there were 8 major and 16 minor complications for a total of 24 complications in 22 patients (Lauter & Froines 2001). There were two deaths in the series, one from an anastomotic leak and the other from intra-abdominal sepsis and multiorgan failure from an unrecognised enterotomy likely during the open portion of her converted sigmoid resection for diverticulitis. The main causes of complications were *C.difficile* colitis (4 cases), incisional hernias (3 cases), urinary retention (2 cases) and another anastomotic leak. There were more major complications including death, anastomotic leak, re-operation or abscess requiring percutaneous drainage in the first 50 cases (n = 3) and in the next 50 cases (n = 3) compared with the last 50 cases (n = 1).

In the study of early versus late experience of laparoscopic colorectal resections, the rate of intra-operative complications was higher for the first 30 cases than for later cases (Schlachta et al 2001). There was a non-significant trend towards declining intra-operative complications rates (9% vs 7%, p = 0.70) comparing early and late experience, with no apparent differences in the type and severity of complications. Post-operative complications occurred with fairly even frequency in early and late experiences. For procedures completed laparoscopically, there was no difference in the rate of post-operative complications between early and late experience (30% vs 32%, p = 0.88). There was also no apparent difference in the distribution of post-operative complications

between early and late experience. The same group of surgeons reported a series of 669 successful laparoscopic colorectal procedures (out of 750) for benign and malignant (49.6%) diseases (Schlachta et al 2003). The post-operative complication rate was 27.5% (184 patients). Most common were minor wound infections. Twenty percent of wound infections occurred in a perineal wound and not at abdominal sites. There were only 7 pulmonary complications (1%). Post-operative ileus and small bowel obstruction occurred with equal frequency (3.9%). The anastomotic leak rate was 2.5% (14 of the 555 laparoscopic procedures in which an anastomosis was performed). Sixteen patients (2.4%) required early re-operation for complications, mostly for anastomotic leak (5 patients) and small bowel obstruction (6 patients). Post-operative mortality was 2.2% (15 patients), predominantly due to myocardial infarction (6 patients) and stroke (2 patients).

In the analysis of caseloads from the COLOR study, six patients out of 536 died during the post-operative period (Kuhry et al 2005). Four of these patients were treated at low volume hospitals ($p = 0.14$). In two of these cases, the death was not related to the surgical procedure. One patient died due to multiorgan failure after an anastomotic leak. In another patient, necropsy revealed a large bleed of undetermined origin. The other causes of death were sepsis, ruptured inflammatory aneurysm, stoke and multiorgan failure of unknown cause. Complications occurred significantly less often at medium and high volume hospitals than in those with a low caseload ($p = 0.006$), particularly pulmonary problems ($p = 0.004$). The number of re-interventions during the first 28 days after surgery showed no significant correlation with hospital caseload ($p = 0.26$). There

were significantly fewer re-admissions to high case volume centres than to hospitals with a medium or low caseloads ($p = 0.01$).

ALSGBI CONCLUSION ON THE INCIDENCE OF SHORT TERM COMPLICATIONS:

LAPAROSCOPIC RESECTION FOR COLORECTAL CANCER IS ASSOCIATED WITH LESS PERI-OPERATIVE MORBIDITY THAN OPEN SURGERY, PARTICULARLY IN THE INCIDENCE OF WOUND INFECTION RATES. INCREASING LAPAROSCOPIC EXPERIENCE MAY REDUCE SHORT TERM MORBIDITIES FURTHER.

10. Incidence of long term complications

Comparative, randomised studies

Incisional hernia, as a delayed complication, was recorded in eight patients (of 203) who underwent laparoscopic rectosigmoid resection and in four (of 200) who had open resection in the RCT from Hong Kong (Leung et al 2004).

In the RCT of 37 laparoscopic versus 46 open colectomy for cancers from St. Louis, incisional hernias developed in 9 patients (24.3%) who underwent laparoscopic colectomy and in 9 patients (19.6%) in the open colectomy group (not significant). The time to hernia development averaged 24.5 months (SD 17, range 3-49) after laparoscopic resection and 16.4 (SD18.3, range 3-60) after open surgery (not significant) (Winslow et al 2002). In the laparoscopic group, only one hernia occurred at a trocar site (umbilical), whereas the rest occurred at extraction sites. The incidence of incisional hernia at the extraction site for laparoscopic resection (21.6%) was not statistically different from that at the midline laparotomy incision for open surgery (19.6%). Incisional hernias developed in 18% of laparoscopic-related suprapubic incisions versus 23% of peri-umbilical sites (non-significant). In the laparoscopic group, 6 patients (16.2%) required operative repair of an incisional hernia. Of the 9 patients in the open colectomy group who developed incisional hernias, 3 (6.5%) have undergone operative repair and an additional 4 were being observed. Of the two remaining patients, one died of a cancer-related death prior to repair. The final patient in the open group with an incisional hernia had a complicated post-operative course with abdominal compartment syndrome

requiring Bogota bag placement and subsequent abdominal wall reconstruction with Vicryl mesh. The abdominal wall defect was later skin grafted and future operative repair was planned. Mean length of follow-up was not significantly different between patients who developed hernias and those who did not (overall 30.1 months, SD 17.8). Patients with hernias had a significantly greater incidence of diabetes mellitus (33%) then those without hernias (13%; p = 0.05).

Comparative, non-randomised studies

In the prospective comparison of laparoscopic versus open resections for colorectal cancer over a 10-year period, 11 (of 172, 6.4%) laparoscopic and 8 (of 172, 4.7%) open patients developed late morbidity (p = 0.48) (Patankar et al 2003). There were 5 anastomotic strictures, 3 small bowel obstructions and 3 incisional hernias for the laparoscopic group; 2 of each of the complications occurred in the open group. The mean follow-up was 52 months (range, 3-120) for the laparoscopic group and 59 months (range, 3-129) for the open group.

In the Parisian study, late complications (> 1 year after surgery) were more frequent in the 83 open procedures than 74 laparoscopic ones (12% vs 5.4%, respectively; p = 0.01) (Champault et al 2002). 4 anastomotic strictures were noted in each group, in addition to 3 small bowel obstructions and 3 incisional hernias in the open group. The median follow-up was 60 months (range 7-125).

In a retrospective analysis of bladder and sexual function before and after laparoscopic (n = 40 patients) or open (n = 40 patients) mesorectal resection for rectal cancer from Sungapore, no significant deterioration in bladder function was observed after a median interval of 3 years (IQR 2-4) (Quah et al 2002). However two patients in the laparoscopic group and none who had an open operation required long-term intermittent self-catheterisation (p = 0.49). One was a 57-year old man who underwent APER for a T3 N2 low rectal cancer, and the other a 41-year old woman who had a low anterior resection for a T3 N1 tumour. Both had normal pre-operative bladder function. A significant difference in male, but not female, sexual function was noted between laparoscopic and open surgery. In the laparoscopic group, five of 15 men who were previously sexually active became impotent after operation, with a further patient reporting moderately impaired erectile function. Among these five men, two had undergone a resection for a locally advanced rectal tumour (T3 N2), one had an APER, one an ultra-low anterior resection, and the other a high anterior resection. In comparison, only one of 22 men in the open surgery group became impotent after operation, with two patients reporting a moderate impairment in erectile function. Similarly there was a significant difference between the two groups in terms of ejaculatory function, with six of 15 men in the laparoscopic group reporting inability to ejaculate after operation, compared with one of 22 in the open group. In the laparoscopic group, of the six men with inability to ejaculate, four were impotent, one had reduction in erectile function, and one had normal erection. In the open operation group, the only patient affected had both erectile and ejaculatory dysfunction. Hence, the overall rate of male sexual dysfunction after operation was seven of 15 in the laparoscopic group compared with one of 22 patients having an open

operation (p = 0.004). This was reflected in the sexual satisfaction score, with a one-point median deterioration in the laparoscopic group, compared with no deterioration in the open group (p = 0.06). Six women in each group were sexually active before operation, and all but one in the open operation group remained sexually active on follow-up. One patient reported increased dyspareunia after laparoscopic approach, but remained sexually active.

In a series of 338 laparoscopic colorectal resections for benign and malignant diseases, incisional or port site hernias were higher in the converted group by 3.5% (Gibson et al 2000).

Non-comparative studies

In the study of 102 patients who underwent laparoscopic colectomies for colorectal cancer from Miami, late complications occurred in 2 patients after a mean follow-up of 64.4 months (Lujan et al 2002). There was one anastomotic stricture requiring balloon dilatation and one ventral hernia at the extraction site.

After a median follow-up of 71 months (range 7-108), one port-site incisional hernia developed from a cohort of 182 patients who underwent laparoscopic colorectal resection for cancer in Brisbane (Lumley et al 2002). One anastomotic stricture was reported in a group of 70 patients who underwent laparoscopic surgery for rectosigmoid and rectal cancers after a median follow-up of 23 months (Yamamoto et al 2002). In another series of 50 laparoscopic resections for stage III colon cancer, 3 late anastomotic strictures were

reported after a median follow-up of 24 months (Franklin et al 2000). All followed anterior resections with low anastomoses and were dilated with temporary ileostomy in one case.

In a series of 194 laparoscopic cancer resections from Berlin, the most common late complication was incisional hernia in 3.6% of the patients after a mean follow-up of 46.1 months (Bärlehner et al 2005). The overall late complication rate was 8.8%, including anastomotic stricture (2.1%), ileus (1.5%) and incontinence (1%).

Seven out of 44 patients developed late complications in a series of laparoscopic TMEs with J-pouch reconstruction for mid and low rectal cancers (Tsang et al 2003). Four patients had minor anastomotic stenosis; all responded to a single dilatation under anaesthesia, and ileostomy closure was not delayed. Two men had persistent erectile dysfunction after operation. One patient had pouch excision and end colostomy formation for late pouch ischaemia. No patient complained of incontinence to solid stool at any time during follow up. One patient suffered from occasional nocturnal soiling up to 24 months after ileostomy closure.

Long-term urinary problems persisted in one man with unilateral pelvic plexus damage from a series of 32 laparoscopic rectal cancer excisions with coloplasty (Rullier et al 2003). Of 18 men who had been sexually active before treatment, ten remained so after the operation; eight of these men had normal ejaculation (median follow-up 6 months).

In the series of laparoscopic left hemicolectomies for cancer, six patients from a group of 166 who underwent curative resections required further surgery because of late complications (4 bowel obstructions, 1 anastomotic stenosis and 1 incisional hernia) (Lechaux et al 2002). The median follow-up was 65 months (SD28, range 12-120). In the palliative resection group (45 patients), 3 patients developed late complications unrelated to their cancer (1 ileal fistula, 1 anastomotic stenosis and 1 incisional hernia).

In the Turin & Aosta series of 108 patients who underwent laparoscopic colorectal resection for benign and malignant diseases, 7 late complications after recovery were noted after a median follow-up of 44 months (Degiuli et al 2004). There were 2 ureteral stenoses, both about 4 months post-operatively, due to retroperitoneal fibrosis. One trocar site hernia (0.9%) and three suprapubic hernias (2.7%) were also recorded.

In the retrospective analysis of 716 patients undergoing laparoscopic or open colectomy and small bowel resection (16 patients in total) for benign and malignant diseases over a median follow-up of 2.5 years, significantly higher incidences of both ventral hernia and small bowel obstruction were noted in the open group (Duepree et al 2003). Five of 211 laparoscopic patients developed hernia compared with 65 of 505 open patients ($p = 0.00002$). The location of the hernias was port site in 4 patients and extraction site in one patient in the laparoscopic group; all hernias in the open group were in the midline wounds. The incidence of surgical repair of ventral hernia was also significantly higher in the open group (28 patients) compared with laparoscopic group (4 patients; $p < 0.05$). Post-operative small bowel obstruction requiring hospitalisation with conservative

management occurred in 4 laparoscopic patients (1.9%) compared with 31 open patients (6.1%; p = 0.01). However there was no difference between surgically treated small bowel obstructions between laparoscopic (3 patients) and open (8 patients) surgery (p = 0.87). The overall re-operation rate for these two complications was almost double in the open group than in the laparoscopic group (7.7% vs 3.8%, respectively; p = 0.03). The incidence of small bowel obstruction and hernia was 23.3% in the open patients with malignant pathologies versus 3.7% in the laparoscopic group, and this was highly significant (p < 0.05). In laparoscopic surgery for malignancies, no hernias were seen, although 13.7% of the open cancer patients developed hernias.

ALSGBI CONCLUSION ON THE INCIDENCE OF LONG TERM COMPLICATIONS:

LAPAROSCOPIC RESECTION FOR COLORECTAL CANCER HAS A TENDENCY FOR LESS LONG TERM MORBIDITIES COMPARED WITH OPEN SURGERY, ESPECIALLY IN THE RATES OF INCISIONAL HERNIATION AND SMALL BOWEL OBSTRUCTION.

11. Length of hospital stay

The bowel cancer study from the Association of Coloproctology of Great Britain and Ireland report a median hospital stay of 11 days (range 0-582) from 10613 cases of bowel cancer (Smith et al 2004).

Meta-analysis

The length of hospital stay was reported in nine studies examined in the meta-analysis from Sydney (Abraham et al 2004). All nine studies report a shorter length of stay after laparoscopic colorectal resection, an improvement of 20.6% (range 13.9-37.5).

Comparative, randomised studies

Hospital stay was significantly shorter ($p = 0.005$) after laparoscopic colorectal cancer resection (mean 5.2 days, SD 2.1) compared with open surgery (mean 7.9 days, SD 9.3) in the RCT from Barcelona (Lacy et al 2002). Similarly in the final results from the COST study, the median duration of stay was 5 days (IQR 4-6) in the laparoscopic group compared with 6 days (IQR 5-7) in the open group ($p < 0.001$) (The COST study group 2004). This was consistent with an earlier analysis of a smaller subset of patients from the same trial that showed a reduction in hospital stay in the laparoscopic group (laparoscopic median 5 days, mean 5.6, SE 0.26 vs open median 6 days, mean 6.4, SE 0.23; $p < 0.001$) (Weeks et al 2002).

In the RCT from Hong Kong, hospital stay was significantly shorter ($p < 0.001$) in laparoscopic rectosigmoid resection (mean 8.2 days, range 2-99) compared with open surgery (mean 8.7 days, range 3-39) (Leung et al 2004).

In the MRC-CLASSIC trial, median stay was 2 days longer for patients allocated open surgery (median 11 days, IQR 8-15) than for those allocated laparoscopic surgery (median 9 days, IQR 7-14) (Guillou et al 2005). Conversion from laparoscopic to open surgery extended hospital stay to a median of 12 days (IQR 9-16). Hospital stay for colonic resections was the same in both treatments (median 9 days). For rectal resections, hospital stay was 2 days shorter for laparoscopic (median 11 days, IQR 9-15) than for open surgery (median 13, IQR 9-18), but for successful laparoscopic-excisions, hospital stay was 3 days shorter than for converted patients (median 10 days, IQR 8-14 vs median 13 days, IQR 11-21, respectively).

In the paper of cost analysis from the COLOR trial, the length of stay in hospital was the same for laparoscopic surgery (mean 9 days, CI 8.0-9.9) and open surgery (mean 9.1 days, CI 8.2-10) (Janson et al 2004).

Hospitalisation was shorter ($p < 0.05$) in laparoscopic colonic resection (mean 5.2 days) compared with open surgery (mean 7.3 days) based on actual treatment analysis (Curet et al 2000). The mean hospital stay for patients whose procedure was converted to open surgery was 8 days. Similarly laparoscopic surgery resulted in shorter stay (mean 5 days, range 3-8) than open surgery (mean 6 days, range 5-9; $p < 0.05$) in the study from Los

Angeles (Kaiser et al 2004). The mean stay for converted patients was 7 days (range 5-13).

In the RCT from Tokyo, laparoscopic colectomy for T2 and T3 cancers resulted in shorter hospital stay (mean 7.1, range 4-15) compared with open surgery (mean 12.7 days, 6-57; $p = 0.01$) (Hasegawa et al 2003).

Similarly, hospitalisation was shorter for laparoscopic surgery (mean 8.1 days, SD 3.1) compared with open surgery (mean 13.3 days, SD 3.4; $p = 0.001$) in the RCT for TME in low rectal cancers from Chengdu (Zhou et al 2004).

In the Sao Paulo RCT of 13 laparoscopic APERs and 15 open APERs, hospital stay was longer for laparoscopic surgery (mean 10.5 days) but this was not significant compared with open APER (data not shown; $p = 0.42$) (Araujo et al 2003).

In the RCT of laparoscopic versus open colorectal surgery for benign and malignant diseases from Milan, the mean length of hospital stay was 10.4 days (SD 2.9, median 8, range 5-83) in the laparoscopic group and 12.5 days (SD 4.1, median 10, range 6-80) in the open group ($p < 0.0001$) (Braga et al 2002). The same authors report similar findings in a study of similar design examining metabolic and functional results after laparoscopic colorectal surgery (laparoscopic: mean 9.1 days (SD 2.9), open: mean 11.7 days (SD 5.1); $p = 0.03$) (Braga et al 2002). It is unclear whether this represents a smaller cohort of the former study.

In the RCT examining functional recovery after colonic resection for benign and malignant diseases, patients stayed a median 2 days after surgery in both laparoscopic and open procedures (mean 3.8 days, range 2-20 and mean 3.9 days, range 2-5 respectively, $p > 0.05$) (Basse et al 2005). One laparoscopic patient had a cerebral infarction at day 2 and was transferred to the neurology department at day 20, where he stayed for rehabilitation until day 155. Only the 20 days in the surgical department was counted in the calculations of total hospitalisation.

Comparative, non-randomised studies

The mean hospital stay was significantly shorter ($p = 0.001$) for patients undergoing laparoscopic surgery (mean 8.2 days, SD 3.4) compared with open resections (mean 12.3 days, SD 3.6) for colorectal cancers in the Parisian study (Champault et al 2002). In the Candiolo study, the post-operative stay was 1 day shorter for laparoscopic (mean 10.5 days, SD 5 & median 9 days) than for open (mean 11.6 days, SD 4.7 & median 10 days) resections ($p = 0.09$) (Capussotti et al 2004).

In the study from Rome/Ancona comparing laparoscopic versus open colectomy for cancers, the mean hospital stay was 9.2 days for laparoscopic and 13.2 days for open right hemicolectomy ($p < 0.001$) (Lezoche et al 2002). The stay for left hemicolectomy was 10.0 days and 13.2 days respectively ($p < 0.001$). The same results were presented in these authors follow-up series (Lezoche et al 2003).

Shorter hospital stay ($p = 0.02$) was also reported for laparoscopic APER (median 16 days, range 7-66) compared with open APER (median 25.5 days, range 10-66) in the study from Hong Kong (Leung et al 2000). Similarly hospital stay was shorter in laparoscopic TME (median 12 days, range 6-50) than open TME (median 19 days, range 3-20; $p = 0.007$) in the Dutch case-control series of rectal cancers (Breukink et al 2005), particularly for low anterior resection (laparoscopic median 11 days, range 6-50 vs open median 19 days, range 8-43; $p = 0.02$). There was no difference in hospital stay for APER (laparoscopic median 21 days, range 11-37 vs open median 33 days, range 11-51; $p = 0.12$).

In the series of 101 laparoscopic rectal excisions for cancer, the mean length of hospital stay was 14.4 days (SD 10.1) compared with 19.9 days (SD 15.7) for open surgery ($p < 0.001$) (Anthuber et al 2003). For 44 laparoscopic TMEs with J-pouch reconstruction, the median hospital stay was 8 days (range 6-26) (Tsang et al 2003). Similarly post-operative stay was significantly shorter ($p < 0.001$) following 32 laparoscopic rectal excisions (median 9 days, range 7-29) compared with 43 open procedures (median 16 days, range 8-57) (Rullier et al 2003). Hospital stay was 2 days shorter after laparoscopic rectal cancer excision (mean 7.8 days, SD 1.5) than open procedure (mean 9.1 days, SD 3.3) but this did not reach significance (Wu et al 2003).

Mean duration of hospitalisation was significantly shorter in laparoscopic (6.9 days, SD 5.4) than open colorectal resection (10.9 days, SD 9.3; $p = 0.003$) in the study from

Hamilton (Hong et al 2001). A total of 12 patients (4 laparoscopic, 8 open) were excluded from this analysis because of prolonged hospitalisation caused by a wait for nursing home placement. The wait for nursing home placement ranged from 35-54 days in the laparoscopic group and 21-121 days in the open group. Inclusion of this group in the analysis showed that duration of post-operative hospitalisation remained significantly shorter in the laparoscopic group (8.2 days, SD 7 vs 12.6 days, SD 13.2, respectively; $p < 0.0001$).

The length of patients' hospital stay was shorter in laparoscopic right hemicolectomy (mean 9.9 days) compared with open surgery (mean 12.8 days) but this trend was not significant ($p = 0.07$) (Baker et al 2004). Similarly stay was shorter in the series from Shanghai and this was significant ($p = 0.04$) (laparoscopic right hemicolectomy mean stay 13.9 days, SD 6.5 vs open right hemicolectomy mean 18.2 days, SD 5.9) (Zheng et al 2005). Post-operative stay was also significantly shorter ($p < 0.01$) after laparoscopic colectomy (mean 16.4 days, SD 5.7, range 10-30) than open surgery (mean 24.6 days, SD 9.7, range 13-39) in the study of Dukes' A cancer from Oita (Kakisako et al 2000).

In the Singaporean experience of 35 laparoscopic colorectal procedures for benign and malignant conditions, the mean hospital stay was 5.3 days (range 2-15) for laparoscopic and 9 days (range 2-62) for open operations ($p < 0.05$) (Koh et al 2005). The mean stay for converted patients was 12.7 days (range 4-27).

In a series of 338 laparoscopic colorectal resections for benign and malignant diseases, the laparoscopic group had a mean shorter hospital stay when compared with the converted group (mean 6 days vs mean 9 days respectively) (Gibson et al 2000).

Non-comparative studies

The mean hospital stay of 220 patients who underwent laparoscopic rectal cancer resection was 6.8 days (SD 4.6, range 1-40) (Delgado et al 2004). In the series of 102 TMEs for rectal cancer from Strasbourg, patients stayed in hospital for an average of 11.9 days (range 5-16) (Leroy et al 2004). This was similar (mean 12 days, range 5-53) to a consecutive series of 100 laparoscopic TMEs for benign and malignant neoplasms from Turin & Aosta (Morino et al 2003). However if the result of one patient who stayed 104 days after a severe fistula and re-operation was included in the analysis, the mean post-operative stay was 16.6 days (SD 9.7, range 5-104). A Brazilian series of 32 laparoscopic TMEs report a mean hospital stay of 5.12 days (range 4-7) (Reis Neto et al 2002). In a series of 82 laparoscopic TMEs with anal sphincter preservation for low rectal cancer, the mean hospital stay was 8 days (range 5-14) (Zhou et al 2004). The median post-operative stay after laparoscopic anterior resection was 6.5 days and 8 days after APER in a series of 80 laparoscopic TMEs (Poulin et al 2002).

In laparoscopic resection for rectosigmoid and rectal cancers, the median hospital stay was 8 days (range 6-34) (Yamamoto et al 2002). There was no statistical difference ($p = 0.11$) between resection for rectosigmoid/upper rectal cancers (median 8 days, range 6-

28) and for middle/lower rectal cancers (median 10 days, range 7-34). In a further series from the same institution, the median length of post-operative hospitalisation was also 8 days for laparoscopic colectomy (range 7-20) and for laparoscopic low anterior resection (range 7-17), with no difference between the two groups ($p = 0.25$) (Yamamoto et al 2004).

The median hospital stay was 6 days (range 3-37) for laparoscopic surgery for stage III colonic cancers (Franklin et al 2000), similar to that of 5 days (mean 5.9, SD 2.5, range 3-23) for colectomies (Jacob et al 2005) and 8 days (range 5-30) for stage I colorectal cancers (Watanabe et al 2003).

In the German five-centre study that examined 399 patients undergoing laparoscopic colorectal cancer resection, the mean post-operative hospital stay was 15.4 days for sigmoid or left colectomy, 14.5 days for anterior resection, 14.3 days for APER and 14 days for right hemicolectomy (Schiedeck et al 2000).

In a series of 108 patients undergoing laparoscopic colorectal resections for benign and malignant conditions, the mean post-operative stay was 7.2 days (Degiuli et al 2004). Patients whose procedure was performed and completed laparoscopically averaged 6.8 days (median 6, range 3-19). Patients converted to open laparotomy were discharged an average of 9.3 days post-operatively (median 8, range 5-32). Patients submitted to right hemicolectomies had the earliest recovery (average 5.8 days) among those receiving an

anastomosis. Patients in whom no anastomosis was performed (diverting colostomies) were discharged after an average of 3.5 days (range 3-4).

In a series of 181 laparoscopic sigmoid colectomies for benign and malignant conditions, the mean length of hospital stay was 2.5 days (SD 1.2) for completed cases and 6.4 days (SD 1.4) for converted cases (Senagore et al 2003).

The median hospital stay was 2.5 days in elderly and high-risk patients whose colonic resection for benign and malignant conditions was completed laparoscopically (Bardram et al 2000). 26 of the 39 patients operated on laparoscopically were discharged on day 2 (17 patients) or day 3 (9 patients). The reasons for staying in hospital beyond the scheduled 2 days included complications (8 patients), difficulty in re-establishing the patient's usual home care service (4 patients), chronic hip arthritis pain (1 patient) and a non-functioning epidural catheter (2 patients) which required treatment with narcotics that results in delayed defaecation. For patients who procedure was converted, the median stay was 10 days (range 5-15) for uncomplicated cases and for two complicated cases, the stay was 37 and 64 days.

In a series of 150 laparoscopic colorectal procedures for benign and malignant diseases, the mean length of post-operative hospital stay for all patients was 4.5 days (range 2-18) (Lauter & Froines 2001). Median day of discharge was post-operative day 4. Mean length of stay and median day of discharge for patients undergoing successful elective laparoscopic resection were 4.2 days (range 2-18) and post-operative day 3, respectively,

including patients with complications. Mean length of stay for converted cases was 7.6 days (range 4-17), with a median day of discharge on post-operative day 7.

Hospital stay was similar for 17 octogenarians who underwent laparoscopic colonic surgery (median 10 days, range 6-28) compared with younger patients (median 9 days, range 7-29; $p = 0.64$) (Yamamoto et al 2003).

In the COLOR study, median time until discharge from hospital was 6, 7 and 8 days for high, medium and low volume hospitals, respectively ($p < 0.001$) (Kuhry et al 2005). Similarly post-operative stay was longest for the first 30 cases in the study from Toronto and Quebec (Schlachta et al 2001). This declined significantly comparing early and late experience (median 6.5 vs 5 days, respectively; $p < 0.001$). The same group of surgeons reported a series of 669 successful laparoscopic colorectal procedures (out of 750) for benign and malignant (49.6%) diseases (Schlachta et al 2003). The median post-operative hospital stay for all procedures was 5 days (range 1-72) with a mode of 4 days. Post-operative length of stay was longer if conversion to open surgery was required than if the laparoscopic approach was successful (median 7 days vs 5 days, $p < 0.001$). Of the 669 patients having successful laparoscopic procedures, 114 (17%) were discharged home within 3 days of surgery, 241 (39%) within 4 days, and 381 (57%) within 5 days. One hundred and fifty three (23%) patients stayed longer than 7 days, 104 (68%) of whom had post-operative complications. Patients having a post-operative complication had a significantly longer hospital stay than those without complications (median 9 days vs 5

days, $p < 0.001$). Median length of post-operative stay declined from 6 days in the first half of the series to 5 days in the second half ($p < 0.001$).

ALSGBI CONCLUSION ON THE LENGTH OF HOSPITAL STAY:

LAPAROSCOPIC COLORECTAL RESECTION RESULTS IN SHORTER HOSPITAL STAY COMPARED WITH OPEN SURGERY.

12. Post-operative and long-term pain

Meta-analysis

Post-operative pain and the requirement for narcotic analgesia following 786 procedures were assessed in 7 trials in the meta-analysis from Sydney (Abraham et al 2004). All trials reported less post-operative pain and requirement for narcotic analgesia in the laparoscopic group. Post-operative pain measured on a visual analogue scale (VAS) at 6-8 hours after completion of surgery was reported in 3 trials (n = 173 patients). Patients in the laparoscopic group reported on average 34.8% (range 15.4-65.6) less pain at rest and 33.9% (range 23.1-50.8) during coughing than those in the open group. On day 1, patients in the laparoscopic group from 4 trials (n = 207 patients) reported 11.6% (range 0-32.7) less pain at rest and 22.2% (range 8.3-37.5) during coughing. On day 2, the figures were 6.8% (range 0-66.7) and 13.1% (range -28.6 to 53.8) respectively (n = 94 patients). On day 3, patients in LR group from 2 trials (n = 94 patients) reported 62.5% (range 50-84.6) less pain at rest and 40.0% (range14.3-54.5) less pain during coughing than those in the open group.

The dose of post-operative narcotic analgesia in milligrams morphine (or equivalent) administered intravenously via a patient-controlled pump was extracted and cumulative requirements for the first 48 hours calculated for 269 patients from 4 trials. In all 4 trials, less narcotic analgesia was required in the laparoscopic group. Patients in the laparoscopic group required 36.9% (range 13.4-72.1) less narcotic analgesia in the first 48 hours than those who had open surgery (n = 269, 5 converted procedures missing).

Comparative, randomised studies

In the COST study, laparoscopic surgery resulted in less duration of use of parenteral analgesics (laparoscopic: median 3 days, IQR 2-4, open: median 4 days, IQR 3-5; $p < 0.001$) and in less duration of use of oral analgesics (laparoscopic: median 1 day, IQR 1-2 vs open: median 2 days, IQR 1-3; $p = 0.02$) (The COST study group 2004). These results were similar to an earlier analysis of a smaller subset of patients from the same study (Weeks et al 2002). However the latter study also examined pain distress scores up to 2 months post-operatively. Two-day post-operative pain distress scores indicated substantial increases in both laparoscopic and open patients. By 2 weeks after surgery, scores had declined to below pre-operative baseline levels. Further improvement was evident at 2 months. There were no significant differences between laparoscopic and open surgery at any time point.

Similarly there was less need for post-operative analgesia in laparoscopic rectosigmoid resections (mean 4.5 injections, range 0-23) compared with open surgery (mean 6.9 injections, range 0-49; $p < 0.001$) (Leung et al 2004). Visual analogue pain score was also lower on post-operative day 1 in the laparoscopic group (laparoscopic: mean 4.6, SD 2.4, open: mean 5.4, SD 2.3; $p = 0.003$).

In the MRC-CLASSIC study, pain scores (EORTC QLQ-C30 scores for symptom scales) were not significantly different between laparoscopic and open resection at baseline, at 2

weeks and at 3 months assessment (Guillou et al 2005). Pain scores rose at 2 weeks but returned to baseline levels at 3 months in both groups.

In the RCT from Los Angeles, the mean use of analgesia was 2 days (range 0-3) in laparoscopic colectomy compared with 4 days (range 2-7; $p < 0.05$) (Kaiser et al 2004). In the converted group, the mean use was 3.5 days (range 1-7).

Similarly analgesic requirement was less in laparoscopic colectomy for T2 and T3 cancers (mean 1.7 days, range 0-4) than in open surgery (mean 3.4 days, range 0-17; $p = 0.002$) (Hasegawa et al 2003). However in TME for rectal cancers, there was no difference ($p = 0.22$) in the use of parenteral analgesics in laparoscopic (mean 3.9 days, SD 0.9) and in open (mean 4.1 days, SD 1.1) resections (Zhou et al 2004).

In the RCT examining metabolic and functional results after colorectal surgery for benign and malignant diseases, good pain control was obtained in both laparoscopic and open surgery at rest and when coughing, with no differences between the groups (Braga et al 2002). This probably reflected the efficacy of patient-controlled administration of analgesia combined with continuous epidural infusion. However, to obtain good pain control, morphine consumption in the first 48 hours after operation was significantly lower after laparoscopic surgery than after open resection ($p = 0.02$).

In another RCT of laparoscopic versus open colonic resection for benign and malignant diseases, patients in the laparoscopic group had a slightly higher ($p < 0.05$) pain score at

rest and during activity compared with the open group on the day of operation and on the first day (data not shown in paper) (Basse et al 2005). From days 2 to 30, there was no difference in pain score between groups ($p > 0.05$).

Comparative, non-randomised studies

In the study of APER from Hong Kong, the post-operative analgesic requirement was significantly less ($p = 0.02$) in laparoscopic APER (median number of injections 5, range 0-36) compared with open APER (median 11, range 0-35) (Leung et al 2000).

Similarly patients undergoing laparoscopic colorectal resections required fewer days on intravenous or intramuscular analgesic therapy compared with open surgery (2.7 days, SD 1.5 vs 3.2 days, SD 2.0, respectively; $p = 0.02$) from the study in Hamilton (Hong et al 2001). The number of days patients required parenteral opiates or continued epidural analgesia was significantly less in laparoscopic right hemicolectomy (mean 2.5 days, median 2.5, SD 5.9) compared with open surgery (mean 4.5 days, median 3, SD 1.8; $p = 0.008$) (Baker et al 2004).

In the series of right hemicolectomies from Shanghai, analgesia requirement was significantly less in the laparoscopic group (mean 14%, SD 46.7) compared with the open group (mean 26%, SD 76.5; $p = 0.01$) (Zheng et al 2005).

In the Singapore experience of laparoscopic colorectal surgery for benign and malignant diseases, analgesia was required for an average of 2.25 days (range 1-7) for those in the

laparoscopic group, compared with 2.64 days (range 1-4) in the open group (p = 0.05) and with 3.43 days (range 2-7) in the converted group (Koh et al 2005).

Non-comparative studies

In the series of 100 laparoscopic TMEs for rectal neoplasms, no patient required narcotics for post-operative pain control (Morino et al 2003). Parenteral non-steroidal analgesics (ketorolac) were required in 27% of cases only up to post-operative day 2. Routinely, epidural local anaesthetics (bupivacaine) were administered for 48 hours post-operatively.

Post-operative analgesic requirement was required in 45 out of 82 patients who underwent laparoscopic TME with anal sphincter preservation for rectal cancers in a series from Chengdu (Zhou et al 2003).

In the German five-centre study that examined 399 patients undergoing laparoscopic colorectal cancer resection, the mean post-opeartive day that analgesics were discontinued was 4.4 days for sigmoid or left colectomy, 5.7 days for anterior resection, 5.6 days for APER and 4.3 days for right hemicolectomy (Schiedeck et al 2000).

The median post-operative pain score after discharge was 1 (slight), and only 5 patients in a group of elderly and high-risk patients undergoing laparoscopic surgery took morphine tablets (10mg) within the 10-day post-operative period (Bardram et al 2000).

ALSGBI CONCLUSION ON POST-OPERATIVE AND LONG TERM PAIN:

LAPAROSCOPIC COLORECTAL RESECTION RESULTS IN LESS POST-OPERATIVE PAIN AND IN LESS REQUIREMENT FOR ANALGESIA COMPARED WITH OPEN SURGERY. THERE IS LESS PUBLISHED EVIDENCE EXAMING LONG TERM PAIN BUT THERE APPEARS TO BE LITTLE DIFFERENCE BETWEEN THE TWO TREATMENT GROUPS.

13. Time to return to usual activities

Comparative, randomised studies

There was a significantly shorter ($p = 0.002$) period of time to resume household activity in 203 laparoscopic rectosigmoid resections (mean 32.2 days, range 4-365) compared with 200 open operations (mean 43.7 days, range 7-198) in the RCT from Hong Kong (Leung et al 2004).

In the RCT of laparoscopic versus open colorectal surgery for benign and malignant diseases, the mean time to recover physical and social activity was 32.1 days (SD 21.6) in the laparoscopic group (n = 136 patients) and 65.3 days (SD 33.2) in the open group (n = 133 patients; $p = 0.0001$) (Braga et al 2002).

Return to normal activities was similar ($p > 0.05$) between open (n = 30 patients) and laparoscopic (n = 30 patients) colonic resection for benign and malignant diseases in the Danish RCT examining functional recovery (Basse et al 2005).

The parameters of early recovery are strongly influenced by societal and economic organization of health care within a community (Veldkamp et al 2004). Only in randomised trials can one assume that these factors are evenly distributed in both groups. The relatively large number of patients in the two former studies suggest that the observed effects are genuine although there are few other corroborating studies.

ALSGBI CONCLUSION ON TIME TO RETURN TO USUAL ACTIVITIES:

LAPAROSCOPIC COLORECTAL RESECTION RESULTS IN AN EARLIER RETURN TO USUAL ACTIVITIES COMPARED WITH OPEN SURGERY.

14. Health-related quality of life

Comparative, randomised studies

In the short-term quality of life (QoL) outcome analysis from the COST study, minimal QoL benefits were found with laparoscopic colectomy for colonic cancer compared with open colectomy (Weeks et al 2002). Of 449 patients, 428 provided QoL data. In the univariate analyses comparing pre-operative scores with follow-up QoL scores (symptom distress scale pain intensity, symptom distress scale summary, QoL index summary and global rating scale scores), the only statistically significant difference between arms was in the global rating scale score at 2 weeks. At that time point, patients assigned to laparoscopic surgery reported slightly better overall QoL. In models examining longitudinal comparisons, only the mean (median) global rating scale scores at 2 weeks post-surgery (76.9 [80] for laparoscopic versus 74.4 [75] for open colectomy) approached statistical significance for the interaction between treatment and assessment time point ($p = 0.009$). Of the 226 patients assigned to laparoscopic surgery for whom information was available, 58 (25.7%) required conversion to open colectomy. Among patients assigned to laparoscopic surgery, patients who required conversion reported slightly poorer QoL for all measures at baseline and every follow-up assessment than patient who received laparoscopic resection. There was substantial temporal variation in total symptom distress in both open and laparoscopic patients. Two-day post-operative scores indicated substantial increases in distress in all groups. By 2 weeks after surgery, scores had declined to below pre-operative baseline levels. Further improvement was evident at 2 months. There was no difference between laparoscopic and open surgery.

However the failure to detect differences between the two groups especially in the 2-day post-operative pain distress scores might have been because patients assigned to open colectomy reported only moderate levels of pain distress (more than 50% of patients report 'mildly distressing' pain at 2 days) (Urbach 2002). Furthermore, both the global rating scale and the QoL Index were not employed during the first 2 post-operative weeks, despite the probability that differences in quality of life are likely to be most evident and most pronounced in the early days after surgery (Veldkamp et al 2004).

In the MRC-CLASSIC study, compliance with QoL questionnaires was high in both treatment groups (562 of 696 [81%] patients at baseline, 454 of 674 [67%] at 2 weeks, and 512 of 658 [78%] at 3 months after surgery) (Guillou et al 2005). Analysis of dropout patterns did not suggest any clear association with failure to complete questionnaires. No differences in any of the scales (EORTC QLQ-C30 & QLQ-CR38) or symptoms were recorded between the treatment groups ($p > 0.01$).

QLQ-C30 scores showed similar patterns between surgery groups. At 2 weeks, scores for global quality-of-life and cognitive functioning fell, and score for pain and appetite loss rose; these values returned to at least baseline values by 3 months. More problems than baseline were reported at 2 weeks and 3 months for role functioning and fatigue. Patients reported fewer problems with diarrhoea after 2 weeks and increased problems with physical and social functioning at 2 weeks. Physical and social functioning scores

returned to baseline values at 3 months in the open surgery group but not in the laparoscopic surgery group.

In QLQ-CR38, many symptoms were reported to be worse at 2 weeks but had either returned to baseline values (for frequency and pain on micturition, buttock pain, dry mouth, taste changes, and body dissatisfaction) or were better than baseline (bloated abdomen and weight loss) by 3 months. Patients reported that they felt less attractive and less feminine or masculine at both follow-up assessments. Bowel movement (without production of stool samples) was improved by 3 months. Patients reported less blood in stool samples at 2 weeks, with substantial improvement by 3 months. Painful bowel movement was worse at 2 weeks but improved by 3 months. 252 of 794 (32%) patients in both treatments had a stoma. The scores for stoma problems were similar at both follow-up assessments. However both QoL questionnaires were again not employed during the first two weeks post-operatively, at the time where maximal differences between the two treatment arms might be expected.

In the RCT of functional recovery after open versus laparoscopic colonic resection for benign and malignant diseases, the fatigue scores were similar in the 2 groups for the entire 4-week period at all assessments (Basse et al 2005). Sleep quality deteriorated slightly during the first post-operative night ($p < 0.05$) in the laparoscopic group. From the second night, there were no differences between groups ($p > 0.05$).

Comparative, non-randomised study

In a case-matched series of patients after laparoscopic (52 patients) and open TME for rectal cancer (according to sex, age, type of resection, time period of surgery, and stage of disease), there was no statistical significant difference between the groups with respect to bladder and sexual dysfunction using the EORTC QLQ-CR38 score (Schiedeck et al 2005).

In a retrospective analysis of 26 laparoscopic colectomies compared with 87 open resections for cancers, both procedures were similarly accepted by patients as a good operation that they would recommend to others (mean 1.105, SD 0.315 vs mean 1.206, SD 0.407 respectively, $p = 0.32$) (Adachi et al 2003). The total QoL was not significantly different between the two groups (mean 10.947, SD 1.682 vs mean 11.809, SD 2.241 respectively, $p = 0.12$) and none of the nine individual questions reached a statistically significant difference between the two groups.

A partially retrospective cohort study from Zurich, Switzerland examined QoL using the Medical Outcomes Survey Short Form-36 (SF-36) questionnaire after laparoscopic and open colorectal surgery for benign and malignant diseases (Sokolovic et al 2004). A total of 169 patients completed the SF-36 health status instrument 2.75 years after the operation. Statistically significant differences were noted between the median scores in the domain of physical functioning (85 in the laparoscopic group vs 68 in the open group, $p < 0.05$), and vitality (85 in the laparoscopic group vs 69 in the open group, $p < 0.05$). This suggested that laparoscopic patients achieved better patient-perceived health status

in the areas of physical functioning and vitality over long term than patients who underwent open surgery.

ALSGBI CONCLUSION ON HEALTH-RELATED QUALITY OF LIFE:

THERE APPEARS TO BE LITTLE DIFFERENCE IN THE POST-OPERATIVE QUALITY OF LIFE BETWEEN LAPAROSCOPIC AND OPEN COLORECTAL CANCER RESECTION. HOWEVER CURRENT QUALITY OF LIFE INSTRUMENTS MAY NOT BE SENSITIVE ENOUGH TO DETECT DIFFERENCES BETWEEN LAPAROSCOPIC AND OPEN SURGERY, PARTICULARLY WHEN EMPLOYED MORE THAN TWO WEEKS POST-OPERATIVELY.

4. COST EFFECTIVENESS

Although the cost effectiveness of laparoscopic colorectal surgery should ideally be expressed in terms of incremental cost per quality-adjusted life year, there are few studies examining cost-related issues with this technique. Evidence in English will be presented in the context of RCTs published since 2000. Two studies examined cost-utility in the short term only but one study also allowed for re-operative costs for post-operative complications up to three months from original surgery. Four additional studies reported cost-utility in the short term in a non-randomised setting of laparoscopic colorectal surgery and will be presented separately.

Comparative, randomised studies

In the RCT from Hong Kong, the direct cost of laparoscopic rectosigmoid resection (US $9297 (SD 2091) was about US $2100 more expensive than open surgery (US $7148 [SD 2164]; $p < 0.001$) (Leung et al 2004). In patients whose operation was converted to open surgery because of local invasion, the direct cost was US $9729 (SD 2854).

The mean hospital charge of laparoscopic colorectal resection was US $931 higher than open surgery in the RCT from Milan (Braga et al 2002). This difference resulted from the additional cost of laparoscopic instruments and devices (US $556 per patient) and from the estimated cost for the longer operative time in the laparoscopic group (US $375 per patient). On the other hand, the mean estimated cost saved by the shorter hospital stay in the laparoscopic group was US $840 per patient (US $400 per day).

A subset of Swedish patients from the COLOR trial was included in a prospective cost analysis (Janson et al 2004). Costs were calculated up to 12 weeks after surgery and all relevant costs were included. However no effects of the procedures, such as quality of life or survival, were taken into account. 210 patients were included in the primary analysis, 98 of whom had laparoscopic resection and 112 had open surgery; 14 converted laparoscopic operations were analysed in the laparoscopic group. Total costs to society did not differ significantly between groups (difference in mean for laparoscopic versus open surgery 1846 euros; $p = 0.10$). The cost of operation was significantly higher for laparoscopic than for open surgery (difference in mean 1171 euros; $p < 0.001$), as was the cost of the first admission (difference in means 1556 euros; $p = 0.01$) and the total cost (excluding productivity loss) to the healthcare system (difference in mean 2244 euros; $p = 0.01$).

The secondary cost analysis, which included 24 patients who were excluded from the primary analysis after randomisation, yielded similar data; figures calculated in the secondary analysis were within a range of -35 to 316 of those in the primary analysis, and the statistical significance of the results remained unchanged.

The costs of extra resources consumed during the first admission and resources used after discharge, because of readmission or re-operations, appeared to be higher in the laparoscopic group. Although there was no difference in complication rates, re-operations were more frequent in the laparoscopic group during the first admission and after

discharge. However, this difference was not tested for statistical significance owing to the small number of observations. The total mean cost, excluding productivity loss, for re-operated patients was 19376 euros (range 5543-49835) for laparoscopic and 13637 euros (range 6080-29305) for open surgery.

Within 12 weeks of surgery for colonic cancer, there was no difference in total costs to society incurred by laparoscopic and open surgery. The laparoscopic procedure, however, was more costly to the healthcare system.

Comparative, non-randomised studies

In a case-matched comparison of financial outcome after laparoscopic (n = 150 patients) and open (n = 150 patients) colorectal surgery for benign and malignant (one third of cases) conditions over a 2-year period, the total direct costs were significantly less ($p = 0.003$) for laparoscopic (median US $3208.5 [IQR 2798.8-4034]) than for open (median US $3654.5 [IQR 2922.3-4787]) surgery (Delaney et al 2003). Although total operating room costs (including labour and supply costs for equipment and consumables) were higher for laparoscopic than open surgery (median US $1784.5 [IQR 1408.8-2097.3] vs median US $1021.5 [IQR 847.3-1219.3], respectively; $p < 0.0001$), the length of stay was significantly lower (median 3 days [IQR 1-65] vs median 6 days [IQR 2-59], respectively; $p < 0.0001$). This resulted in significantly lower pharmacy (median US $269 [IQR 209-364] vs median US $432.5 [IQR 330.5-612.3], respectively; $p < 0.0001$), laboratory (median US $64 [IQR 51-101.5] vs median US $122.5 [IQR 83.8-213], respectively; $p < 0.0001$) and ward nursing (median US $674 [IQR 464-995.5] vs median

US $1476 [IQR 1075.3-2038.3], respectively; p < 0.0001) costs. Anaesthesia and intensive care unit nursing costs for both groups were similar.

In the Zurich study of laparoscopic and open colorectal procedures for benign and malignant diseases, the operating room costs for sigmoidectomy, low anterior resection and hemicolectomy were more expensive for laparoscopic than open surgery (laparoscopic: 8864.4 euros, 12056.4 euros, 7218.1 euros, respectively vs open: 7969.2 euros, 11090.75 euros, 6020.6 euros, respectively) (Sokolovic et al 2004). However hospital costs for the surgical ward per surgical intervention were less in the laparoscopic group than the open group in all three operations (laparoscopic: 7265.95 euros, 5707.25 euros, 4150.1 euros, respectively vs open: 8498.1 euros, 8719.9 euros, 5495.2 euros, respectively), predominantly due to a shorter hospital stay in the laparoscopic group (laparoscopic median 11 days, IQR 9-15 vs open median 16 days, IQR 13-23; p < 0.0001). Furthermore laparoscopy required one surgeon less per procedure and led to additional cost savings of 150 euros per median operation time of 175 mins for laparoscopy, according to the calculation of 0.85 euros pre minute/person. Therefore the total hospitalisation cost for laparoscopic surgery was cheaper than open surgery in terms of basic insurance costs (laparoscopic [n = 106] median 2952 euros, IQR 2100-4088 vs open [n = 88] median 4315 euros, IQR 3179-6586; p = 0.0001) and supplemental insurance costs (laparoscopic [n = 90] median 15182 euros, IQR 11326-19000 vs open [n = 42] median 17818 euros, IQR 14541-23774; p = 0.05).

In the Shanghai study of 30 laparoscopic and 34 open right hemicolectomies, the operative cost was RMB yuan 7810.7, SD 1719.0 for laparoscopic surgery compared with RMB yuan 5018.9, SD 845.6 for open surgery ($p < 0.01$) (Zheng et al 2005). However the cost of drugs in the laparoscopic group (RMB yuan 3687.8, SD 1977.4) was significantly less than that in the open group (RMB yuan 5209.4, SD 2212.3) ($p = 0.03$). No significant differences was observed in the total cost of operation and drugs between the two groups (RMB yuan 11498.5, SD 2618.8 vs RMB yuan 10228.3, SD 2372.5, respectively; $p = 0.13$).

In a series of 338 laparoscopic colorectal resections for benign and malignant diseases, mean cost of hospital stay for the laparoscopic group was US $5000 less on average when compared with cost for the converted group (mean US $22000 vs mean US $27000 respectively) (Gibson et al 2000). However patients with a long, complicated hospital course (which included patients from both groups), were omitted from the data reflecting hospital stay, diet and cost.

ALSGBI CONCLUSION ON COST EFFECTIVENESS:

THE OPERATIVE COSTS FOR LAPAROSCOPIC RESECTION OF COLORECTAL CANCER ARE HIGHER BECAUSE OF LONGER OPERATING TIME AND THE USE OF MORE EXPENSIVE DEVICES. HOWEVER THESE COSTS ARE OFFSET BY SHORTER HOSPITAL STAY, LESS USE OF ANALGESIA, LESS USE OF BLOOD PRODUCTS AND LESS COMPLICATIONS IN THE SHORT AND LONG TERM.

5. INFLUENCE OF ENHANCED RECOVERY PROGRAMMES

Enhanced recovery programmes have been popularised by Kehlet from Copenhagen, Denmark (Basse et al 2004). Fast-track rehabilitation involves continuous epidural analgesia, enforced oral nutrition, mobilisation and planned early discharge. It appears to reduce the hospital stay for patients undergoing colonic resection from about 10 days to 2 or 3 days. In a retrospective study of patients undergoing open colonic surgery, 130 patients receiving conventional care from one hospital were compared with 130 patients receiving multimodal, fast-track rehabilitation in another hospital (Basse et al 2004). Time to first defaecation, hospital stay and morbidity appeared to be reduced after multimodal rehabilitation. Similar results were reported from a retrospective review of 451 patients from 5 European centres (conventional care: Sweden n = 109 patients, UK n = 87 patients, Netherlands n = 76 patients, Norway n = 61 patients and fast-track surgery: Denmark n = 118) (Nygren et al 2005). Rapid rehabilitation was also possible in elderly and high-risk patients who successfully undergo laparoscopic colonic resection (Bardram et al 2000). Furthermore fast-track rehabilitation results in earlier resumption of normal activities with reduced fatigue and need for sleep postoperatively compared to conventional care, and without increased need for nursing care or visits to general practitioners in a prospective, non-randomised study of 30 patients in each group (Hjort Jakobsen et al 2004). However, readmissions may occur more frequently.

In a randomised, observer-and-patient, blinded trial, 60 patients (median age 75 years) underwent elective laparoscopic (n = 30) or open (n = 30) colonic resection for benign and malignant diseases with fast-track rehabilitation and planned discharge after 48 hours. Functional recovery was assessed in detail during the first post-operative month (Basse et al 2005). Median post-operative hospital stay was 2 days in both groups, with early and similar recovery to normal activities as assessed by hours of mobilisation per day, computerised monitoring of motor activity assessed, pulmonary function, cardiovascular response to treadmill exercise, pain, sleep quality, fatigue, and return to normal gastrointestinal function. There were no significant differences in post-operative morbidity or readmissions. No patient died in the laparoscopic group whereas 3 patients died in the open group (10%) - a higher than expected mortality rate. Two of the patients who died were not included in the analysis of hospital stay. If these 2 patients had not died but survived their severe cardiopulmonary problems, inclusion of their subsequent hospital stay might have extended the overall stay in the open group.

Furthermore 30% of patients and 41% of relatives in the open group found the hospital stay to be too short, compared with 17% and 21%, respectively, in the laparoscopic group ($p > 0.05$). This suggests that although rapid functional recovery is possible after open surgery using a multimodal rehabilitation regimen, the use of laparoscopic technique in the same environment is more acceptable to the patients and their carers.

In another non-randomised, prospective, controlled study comparing standard care with multimodal rehabilitation programme in the setting of laparoscopic sigmoidectomy for

benign and malignant conditions, 23 fast-track patients were discharged on day 4 (range 3-6) compared with day 7 (range 4-14) in 29 standard care patients ($p < 0.01$) (Raue et al 2004). On the 1st post-operative day, forced vital capacity was improved ($p = 0.02$) in fast-track patients, but no further differences between both groups were detected. Normal gastrointestinal function was achieved early in both groups, but fast-track patients returned to a regular hospital diet earlier than patients receiving standard care ($p < 0.01$). Defaecation also occurred earlier ($p < 0.05$) in the fast-track group. Visual analogue scale scores for pain during rest or coughing were similar for the two groups ($p > 0.05$), but fatigue was increased in the standard-care group on the 1st ($p = 0.06$) and 2nd ($p < 0.05$) post-operative days. Morbidity was not different for the two groups (standard care 22%, fast-track 4%) and there were no deaths in either group. Fast-track patients also felt ready for earlier discharge than standard care patients. Within 30 days after surgery, 1 patient (4%) of the standard group (local wound infection) and 2 fast-track patients (7%) were readmitted. Readmission of both fast-track patients occurred for minor reasons (1 general malaise, 1 gastroenteritis), and neither patient required specific therapy. These data suggest that multimodal rehabilitation can further improve on the results of laparoscopic sigmoidectomy and decrease the post-operative hospital stay.

ALSGBI CONCLUSION ON INFLUENCE OF ENHANCED RECOVERY PROGRAMMES:

THE ADDITION OF MULTIMODAL REHABILITATION PROGRAMME IN THE PRESENCE OF LAPAROSCOPIC COLORECTAL CANCER SURGERY MAY FURTHER IMPROVE SHORT TERM RECOVERY AND REDUCE

HOSPITAL STAY. BOTH METHODS ARE COMPLEMENTARY TO EACH OTHER AND NOT MUTUALLY EXCLUSIVE. FURTHER HIGH QUALITY, LARGE SCALE TRIALS ARE REQUIRED TO DETERMINE THEIR INDIVIDUAL AND COMBINED EFFECTS ON RECOVERY AFTER LAPAROSCOPIC COLORECTAL CANCER SURGERY.

6. WIDER IMPLICATIONS FOR THE NATIONAL HEALTH SERVICE

It is evident that there are many advantages for the patient undergoing laparoscopic colorectal surgery, including less post-operative pain, less use of analgesia, less blood loss, less use of blood products, less short and long term complications, shorter hospital stay and quicker return to usual activities. Although the immediate costs to the National Health Service are higher in laparoscopic than open surgery, overall cost to society remains similar.

Increasingly patients are likely to request minimally invasive surgery for colorectal cancer, particularly when they realise that it is associated with faster recovery without compromising their safety (Solomon et al 2003). They should be given the opportunity of undergoing either laparoscopic or open procedures after careful counseling and informed consent. It is therefore important that there is clear guidance from NICE to the scope of laparoscopic colorectal surgery, particularly in preceptorship training and individual surgeons' auditing of their results.

7. CONCLUSIONS AND RECOMMENDATIONS

This document identifies the many advantages of laparoscopic compared with open resection for colorectal cancer. Furthermore there was no evidence of reduction in long term survival time or increase in the incidence of recurrence or port site metastases. The quality of studies and reporting of data have improved since the last NICE guidance in 2000. In particular high quality evidence from many randomised controlled trials with long term outcomes and one meta-analysis have become available.

The Association of Laparoscopic Surgeons of Great Britain and Ireland recommends that laparoscopic colorectal resection for cancer should be made available to suitable patients and performed by appropriately trained surgeons outside of a randomised controlled trial. It is likely that many colorectal resections will continue to be performed by the open technique because of the current lack of surgical expertise in the UK. However this is not a reason to deny surgeons with the necessary skills the choice of how they perform the operation; neither should patients be denied the proven advantages of the laparoscopic approach. We do not feel that there is a place for exclusion of a technique of proven benefit and superiority over conventional method on the basis of increased operative costs and inadequacy of training. Furthermore the overall cost to society is likely to be the same as open surgery.

We would however urge established consultants without prior laparoscopic colorectal surgery experience to undertake a preceptorship programme before commencing

independent procedures (Kennedy et al 2005). Furthermore all surgeons undertaking laparoscopic colorectal surgery should maintain a careful prospective audit of these procedures, particularly long term outcome results. The data should be entered in the Association of Coloproctology of Great Britain and Ireland database and reviewed by the preceptored surgeons' peers at their local hospital multi-disciplinary meeting. Data should be audited locally in line with advice regarding introducing new techniques.

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