Multimodality Treatment of Colorectal Cancer

Recent Issues in Surgery for Colorectal Cancer

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University of Michigan
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I, my spouse, or any immediate member of my household, do not have any financial interest, arrangement, or affiliation with any company whose products might be discussed in this presentation.

James A. Knol, M.D.
Colorectal Cancer (CRC)

• 4th most frequently diagnosed cancer in US
• 2nd most common cancer causing death in US
• In 2009 in US, predicted 106,000 cases colon cancer and 40,900 cases rectal cancer, with about 49,900 deaths fr CRC
Recent Issues in Surgery for Colorectal Cancer

• Rectal Cancer
  – Staging rectal cancer
  – Total mesorectal excision (TME)
  – Neoadjuvant radiochemotherapy
  – Diversion vs no diversion after pelvic radiotherapy
  – Transanal resection

• Colon and rectal surgery
  – Laparoscopic colon and rectal resection
  – Genetic considerations
Rectal Adenocarcinoma

Avoidance of local recurrence
Factors Increasing Risk of Local Recurrence of Rectal Cancer

- Circumferential margin on tumor $\leq 2$ mm
- Pathologic stage
- Perineural invasion
- Blood vessel invasion
- Age
- Male gender
AJCC Staging
Rectal Adenocarcinoma

• Stage I - Confined to bowel wall, no LN
  – T1 (submucosa)
  – T2 (in muscularis propria)

• Stage II - Through bowel wall, no LN

• Stage III - +LN
Preoperative Staging of Rectal Cancer

• Staging modalities
  – Ultrasonography - transrectal or endoscopic rectal
  – MRI - high resolution or rectal coil
• Similar accuracy
  – T ~80%
  – N (60-70%)
Preoperative Staging of Rectal Cancer

- High-resolution pelvic MRI
  - Ability to view the boundaries of the mesorectal fascia
  - Assessment of potential radial margin risk
  - Does not evaluate the T stage per se
Factors Decreasing Risk of Local Recurrence of Rectal Cancer

• Total mesorectal excision

• Pelvic radiotherapy

• Pelvic radiochemotherapy
Total Mesorectal Excision (TME) for Rectal Cancer

• Definition: Sharp dissection (diathermy or scissors) of an intact package of the mesorectum under direct vision

• Not that new - first introduced in 1979 by R.J. Heald - but dissemination takes time

• Like many new concepts, acceptance was based upon verification of advantages of the technique in multiple studies
The mesorectum in rectal cancer surgery—the clue to pelvic recurrence?

Five cases are described where minute foci of adenocarcinoma have been demonstrated in the mesorectum several centimetres distal to the apparent lower edge of a rectal cancer. In 2 of these there was no other evidence of lymphatic spread of the tumour. In orthodox anterior resection much of this tissue remains in the pelvis, and it is suggested that these foci might lead to suture-line or pelvic recurrence. Total excision of the mesorectum has, therefore, been carried out as a part of over 100 consecutive anterior resections. Fifty of these, which were classified as ‘curative’ or ‘conceivably curative’ operations, have now been followed for over 2 years with no pelvic or staple-line recurrence.
Why TME?

- Cancer is confined to the mesorectum in about 85% of patients with rectal cancer.
- TME was found to markedly decrease the local recurrence rate for rectal cancer.
Why TME?

• Before TME, local recurrence at 5 years for rectal cancer treated with anterior resection was 25% with RT alone, 13.5% with radiochemotherapy (NCCTG data - Moertel, 1990)

• With TME, without radiotherapy, 5-year local recurrence for anterior resection
  
  Macfarlane and Heald, 1993  5%
  Enker, 1995  7.5%
  Peeters, 2007  10.9%
TME vs NCCTG Data

<table>
<thead>
<tr>
<th></th>
<th>Local recurrence</th>
<th>Overall recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>TME</td>
<td>5%</td>
<td>22%</td>
</tr>
<tr>
<td>Conventional surgery + radiation therapy</td>
<td>25%</td>
<td>62.7%</td>
</tr>
<tr>
<td>Conventional surgery + chemotherapy + radiation therapy</td>
<td>13.5%</td>
<td>41.5%</td>
</tr>
</tbody>
</table>

Local and total recurrence rates for TME and NCCTG data

Fr. Macfarlane et al. Lancet 1993
Mesorectum Anatomy

Mesorectum: a fatty tissue envelope containing the rectum, its blood vessels and lymphatics, lymph nodes, and associated with the pelvic autonomic nerves.
Total Mesorectal Excision

For upper rectal cancers, transection of mesorectum should be at least 5 cm below the lowest extent of the rectal mass

Mesorectum Anatomy

• Posterior: defining visceral fascia is anterior to the Waldeyer’s fascia plane (posterior parietal connective tissue layer adherent to sacrum)
• Anterior: at Dennonvillier’s fascia in the male (posterior to the prostate gland)
• Superior: the aortic bifurcation
• Inferior: the anus
Mesorectum Anatomy

• Associated autonomic nerves
  – Paired hypogastric nerves, arise from sympathetic hypogastric preaortic plexus, from L2 and L3
  – Sacral splanchnic nerves, arise from S2 and S3, are parasympathetic
  – Hypogastric nerves join the sacral splanchnic nerves to form the inferior hypogastric plexus (just lateral and posterior to the seminal vesicles in the male)
TME - The anterior anatomic associations in the male

Neurovascular bundle
S. vesical artery
Right ureter
Inf. Hypogastric plexus
Adequacy of mesorectal excision

Fr. Garcia-Granero et al.  Cancer 2009

FIGURE 1. The definitions used to judge mesorectum in sphincter-saving procedure specimens are illustrated. (A) A complete mesorectum shows good bulk of mesorectum with smooth surface and no defects on mesorectum. (B) A nearly complete mesorectum shows good bulk of mesorectum, but some defects or irregularities in the surface (arrows) are present. (C) An incomplete mesorectum shows a deep defect on the mesorectum under the peritoneal reflection that allows visualization of the muscularis propria (arrow).
Adequacy of mesorectal excision

Fr. Garcia-Granero et al. Cancer 2009
Pelvic Sidewall Dissection

• Cancer is found in the “pelvic sidewall” in about 15% of patients

• Risk factors for pelvic sidewall tumor
  – Female gender
  – Poorly differentiated primary
  – Perirectal lymph node metastases

• No difference in local recurrence without or with sidewall dissection (10.5% vs 7.5%, NS) (Kobayashi H, 2009)
FIGURE 1. A schema of the lateral pelvic area: (A) internal iliac area distal to superior vesical artery and (B) proximal to superior vesical artery, (C) obturator area, (D) external iliac area, (E) common iliac area, and (F) aortic bifurcation area.
With minimal local recurrence rate with TME, is there still a role for pelvic radiotherapy for rectal cancer?
Is there still a role for pelvic radiotherapy for rectal cancer?

Table 1 — Local recurrence rates for different stages of rectal disease

<table>
<thead>
<tr>
<th>Trial</th>
<th>Stage</th>
<th>Radiotherapy and surgery</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swedish Rectal Cancer</td>
<td>I</td>
<td>4.5</td>
<td>14</td>
</tr>
<tr>
<td>Trial [6]</td>
<td>II</td>
<td>6</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>23</td>
<td>46</td>
</tr>
<tr>
<td>Dutch Total Mesorectal Excision Trial [20]</td>
<td>II</td>
<td>1</td>
<td>5.7</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>4.3</td>
<td>15</td>
</tr>
<tr>
<td>Lancet Review [1]</td>
<td>I</td>
<td>3.5</td>
<td>10.4</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>9.8</td>
<td>19.9</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>12.9</td>
<td>27.3</td>
</tr>
</tbody>
</table>

The TME Trial After a Median Follow-up of 6 Years

Increased Local Control But No Survival Benefit in Irradiated Patients With Resectable Rectal Carcinoma

Koen C.M.J. Peeters, MD,* Corrie A.M. Marijnen, MD, PhD,†† Iris D. Nagtegaal, MD, PhD,§
Elma Klein Kranenburg, MSc,* Hein Putter, MD,‖ Theo Wiggers, MD, PhD,¶
Harm Rutten, MD, PhD,** Lars Puhlman, MD, PhD,*** Bengt Gl Cleius, MD, PhD,†††§§
Jan Willem Leer, MD, PhD, and Cornelis J.H. van de Velde, MD, PhD,*
for the Dutch Colorectal Cancer Group

Objectives: To investigate the efficacy of preoperative short-term radiotherapy in patients with mobile rectal cancer undergoing total mesorectal excision (TME) surgery.

Summary Background Data: Local recurrence is a major problem in rectal cancer treatment. Preoperative short-term radiotherapy has shown to improve local control and survival in combination with conventional surgery. The TME trial investigated the value of this regimen in combination with total mesorectal excision. Long-term results are reported after a median follow-up of 6 years.

Methods: One thousand eight hundred and sixty-one patients with patients with nodal involvement, for patients with lesions between 5 and 10 cm from the anal verge, and for patients with uninvolved circumferential resection margins.

Conclusions: With increasing follow-up, there is a persisting overall effect of preoperative short-term radiotherapy on local control in patients with clinically resectable rectal cancer. However, there is no effect on overall survival. Since survival is mainly determined by distant metastases, efforts should be directed towards preventing systemic disease.

What about chemoradiotherapy for rectal cancer?

• EORTC 2291 and FFDC 2903 Trials
• Preoperative radiochemotherapy (FU/LV + 4500 cGy + 900 cGy boost) vs. preoperative radiotherapy alone

<table>
<thead>
<tr>
<th></th>
<th>Local recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiochemotherapy</td>
<td>8 - 9%</td>
</tr>
<tr>
<td>Radiotherapy alone</td>
<td>17%</td>
</tr>
</tbody>
</table>

Preoperative vs Postoperative Radiotherapy in Rectal Cancer

Advantages of preoperative radiotherapy

- Decreased injury to small bowel
- Higher likelihood of completing radiotherapy
- Possibly more effective in well oxygenated tissue
- May increase resectability
- Decreased pelvic recurrence rate*
- May increase chances of sphincter-sparing resection

Preoperative vs Postoperative Radiotherapy in Rectal Cancer

Disadvantages of preoperative radiotherapy

- Possibility of over-treating early stage tumors not requiring radiotherapy
- Possibly increased risk of anastomotic leak
- Does not increase the distance factor from the anal verge, i.e. cannot convert a patient requiring APR because of low-lying tumor to being able to have an LAR
Preoperative Radiotherapy for Rectal Cancer

• Indications
  – T3-4 or N1-2 disease in mid and low rectal cancer
  – Bulky cancer, to decrease tumor size
  – To allow sphincter preservation?

• Contraindications
  – Previous pelvic radiotherapy
  – Open pelvic wounds
Preoperative versus Postoperative Chemoradiotherapy for Rectal Cancer

Rolf Sauer, M.D., Heinz Becker, M.D., Werner Hohenberger, M.D., Claus Rödel, M.D., Christian Wittekind, M.D., Rainer Fietkau, M.D., Peter Martus, Ph.D., Jörg Tschmelitsch, M.D., Eva Hager, M.D., Clemens F. Hess, M.D., Johann-H. Karstens, M.D., Torsten Liersch, M.D., Heinz Schmidberger, M.D., and Rudolf Raab, M.D., for the German Rectal Cancer Study Group*

ABSTRACT

BACKGROUND
Postoperative chemoradiotherapy is the recommended standard therapy for patients with locally advanced rectal cancer. In recent years, encouraging results with preoperative radiotherapy have been reported. We compared preoperative chemoradiotherapy with postoperative chemoradiotherapy for locally advanced rectal cancer.
Cumulative local recurrences among 799 patients

Cumulative distant recurrences among 799 patients

Should the fecal stream be diverted by loop ileostomy or loop colostomy after a low pelvic anastomosis?
Diversion for Low Rectal Anastomosis

• Diversion is used to protect an anastomosis at risk
• Diversion for a rectal anastomosis was not a part of routine practice in past
• Diversion accomplished by:
  – Colostomy with Hartmann’s rectal pouch
  – Loop colostomy, usually a transverse colostomy
  – Loop ileostomy
Diversion for Low Rectal Anastomosis

Risk factors for leak

– Adverse intraoperative events

– Low anastomoses

– Preoperative radiotherapy
Is diversion after low anterior anastomosis indicated?

• Matthiessen et al 2007, Ann Surg
  – Randomized multicenter study; 79% had preop radiotx
  – 234 patients randomized to defunctioning loop stoma or no stoma after low anterior resection - loop ileostomy vs loop transverse colostomy was surgeon’s choice
  – Criteria: anastomoses <=7 cm above anal verge, neg leak test, intact stapler rings, no intraop adverse events
  – Total leak rate 19.2%
    • W/ stoma 10.3%
    • W/O stoma 28.0%
  – At median of 42 months follow up, 13.8% of stoma group and 16.9% of non-stoma group had a stoma (NS)
Is diversion after low anterior anastomosis after radiotherapy indicated?

  - Cases taken from Swedish Rectal Cancer Registry
  - Case control study - 2 controls (268) for each case of leakage (134 pts)
  - Diverting stoma was protective from leakage [OR=0.68 (95% CI 0.52-0.88]

  - Randomized controlled pilot study
  - 34 patients, randomized to stoma group (18) or non-stoma group (16)
  - Symptomatic leaks: 5.5% stoma group - 37.5% non-stoma group (P=0.02)

  - Meta-analysis of randomized controlled trials (5) and observational studies (7) comparing loop ileostomy to transverse loop colostomy for diversion
    - Loop ileostomy - lower risk of prolapse, sepsis
    - Loop ileostomy - higher risk of occlusion after stoma closure, dehydration
What about Stage I Rectal Cancer?

*Is transanal excision of rectal cancer an option?*
Transanal Resection of Rectal Cancer

• Traditional Indications
  – Patient refuses APR, or medically cannot tolerate APR
  – Decrease risk of complications

• Traditional Contraindications
  – Poorly differentiated adenocarcinoma
  – Upper extent of tumor > 8 cm from anal verge
  – Tumor > 1/3 circumference of lumen
  – Tumor > 3 cm diameter
  – Tumor fixed
Transanal Excision of Rectal Cancer

Advantages

- Preservation of anal continence, urinary function, sexual function
- Avoidance of transabdominal operation with attendant morbidity
- Minimal morbidity and mortality

Disadvantages

- Risk of pelvic recurrence
- Risk due to understaging tumor
  - T1 - + LN in 8% (upper third) to 34% (lower third)*
  - T1 - + LN in 23% Haggitt level 3 tumors*
  - T1 - + LN in 11% without lymphovascular invasion*

Conditions for Transanal Excision
Rectal Cancer

- Tumor stage T1 N0 (on a trial, T2 N0)
- Tumor < 3 cm in size
- Well to moderately differentiated
- Upper end of tumor < 8 cm from anal verge
- Able to achieve negative margins (>2 or >3 mm)
- Tumor <= 1/3 circumference of the lumen
- Full-thickness excision
T1-T2, N0 Rectal Cancer

After transanal excision
- pT1 NX, margins neg -> Observe
- pT1-2 NX, high risk features -> transabdominal resection
  High Risk Features
  • poor differentiation
  • lymphovascular invasion
  • margins positive or indeterminate
- pT2 NX
  • Transabdominal resection
  • or, chemoRT, then consider systemic chemo
Laparoscopic Surgery for Colorectal Cancer
Laparoscopic Surgery for Colorectal Cancer

• Criteria of acceptability
  – Oncologic outcomes must be no worse than with open operations
    • Ability to achieve margins and lymph node clearance
    • No different negative oncologic problems (such as port-site implantation)
  – Complication rate and mortality rate must be no worse than with open operations
A Comparison of Laparoscopically Assisted and Open Colectomy for Colon Cancer

The Clinical Outcomes of Surgical Therapy Study Group*

ABSTRACT

BACKGROUND
Minimally invasive, laparoscopically assisted surgery was first considered in 1990 for patients undergoing colectomy for cancer. Concern that this approach would compromise survival by failing to achieve a proper oncologic resection or adequate staging or by altering patterns of recurrence (based on frequent reports of tumor recurrences within surgical wounds) prompted a controlled trial evaluation.

METHODS
We conducted a noninferiority trial at 48 institutions and randomly assigned 872 patients with adenocarcinoma of the colon to undergo open or laparoscopically assisted colectomy performed by credentialed surgeons. The median follow-up was 4.4 years. The primary end point was the time to tumor recurrence.

RESULTS
At three years, the rates of recurrence were similar in the two groups — 16 percent among patients in the group that underwent laparoscopically assisted surgery and 18 percent among patients in the open-colectomy group (two-sided P=0.32; hazard ratio for recurrence, 0.86; 95 percent confidence interval, 0.63 to 1.17). Recurrence rates in surgical wounds were less than 1 percent in both groups (P=0.50). The overall survival rate at three years was also very similar in the two groups (86 percent in the laparoscopic-surgery group and 85 percent in the open-colectomy group; P=0.51; hazard ratio for...
COST Study - 2004

- Colon cancer - a randomized non-inferiority study - 48 institutions, 872 patients
- Median f/u 4.4 years
- Primary endpoint - time to tumor recurrence

<table>
<thead>
<tr>
<th></th>
<th>lap</th>
<th>open</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence at 3 yr</td>
<td>16%</td>
<td>18%</td>
</tr>
<tr>
<td>Survival at 3 yr</td>
<td>86%</td>
<td>85%</td>
</tr>
</tbody>
</table>

Similar mortality and morbidity rates
Less than 1% wound tumor implants for each group
COST Study 2007

- Same patient group, follow up for 8 years, 5-yr data on 90% of patients

<table>
<thead>
<tr>
<th></th>
<th>lap</th>
<th>open</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence</td>
<td>19.4%</td>
<td>21.8%</td>
</tr>
<tr>
<td>Disease-free 5-yr survival</td>
<td>69.2%</td>
<td>68.4%</td>
</tr>
<tr>
<td>Overall 5-yr survival</td>
<td>76.4%</td>
<td>74.6%</td>
</tr>
</tbody>
</table>

Similar sites of first recurrence,

Randomized Trial of Laparoscopic-Assisted Resection of Colorectal Carcinoma: 3-Year Results of the UK MRC CLASICC Trial Group

David G. Jayne, Pierre J. Guillou, Helen Thorpe, Philip Quirke, Joanne Copeland, Adrian M.H. Smith, Richard M. Heath, and Julia M. Brown

ABSTRACT

Purpose
The aim of the current study is to report the long-term outcomes after laparoscopic-assisted surgery compared with conventional open surgery within the context of the UK MRC CLASICC trial. Results from randomized trials have indicated that laparoscopic surgery for colon cancer is as effective as open surgery in the short term. Few data are available on rectal cancer, and long-term data on survival and recurrence are now required.
# Open vs Laparoscopic Rectal Surgery

794 patients, 268 open, 526 lap; rectal: 87 open, 161 lap

<table>
<thead>
<tr>
<th></th>
<th>open(%)</th>
<th>lap(%)</th>
<th>signif</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Local recurrence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>7.9</td>
<td>8.6</td>
<td>NS</td>
</tr>
<tr>
<td>Colon</td>
<td>6.0</td>
<td>7.3</td>
<td>NS</td>
</tr>
<tr>
<td>Rectal, AR, APR</td>
<td>10.1</td>
<td>9.7</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Distant recurrence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>14.3</td>
<td>15.2</td>
<td>NS</td>
</tr>
<tr>
<td>Colon</td>
<td>12.5</td>
<td>11.3</td>
<td>NS</td>
</tr>
<tr>
<td>Rectal, AR, APR</td>
<td>16.4</td>
<td>18.6</td>
<td>NS</td>
</tr>
</tbody>
</table>

Laparoscopic resection of rectosigmoid carcinoma: prospective randomised trial

Ka Lau Leung, Samuel P Y Kwok, Steve C W Lam, Janet F Y Lee, Raymond Y C Yiu, Simon S M Ng, Paul B S Lai, Wan Yee Lau

Summary

Background Although laparoscopic resection of colorectal carcinoma improves post-operative recovery, long-term survival and disease control are the determining factors for its application. We aimed to test the null hypothesis that there was no difference in survival after laparoscopic and open resection for rectosigmoid cancer.

Methods From Sept 21, 1993, to Oct 21, 2002, 403 patients with rectosigmoid carcinoma were randomised to receive either laparoscopic assisted (n=203) or conventional open (n=200) resection of the tumour.

Introduction

Surgeons have attempted a laparoscopic approach in almost every type of operation, and many techniques have quickly become accepted.1 However, most of these developments were not based on reliable evidence from comparative studies.2

Colorectal cancer is one of the commonest malignant diseases worldwide, and laparoscopic resection of colorectal cancer has been used since 1991.3 However, because of early port site recurrence associated with this procedure, most hospital authorities were concerned about the adequacy of tumour clearance and long-term survival after laparoscopic resection.4 Yet surgeons were
## Open vs Laparoscopic Rectal Surgery

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopic group</th>
<th>Open resection group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation time (min)</td>
<td>189.9 (55.4)</td>
<td>144.2 (57.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Blood loss (mL)</td>
<td>169 (0–3000)</td>
<td>238 (0–5836)</td>
<td>0.06</td>
</tr>
<tr>
<td>Postoperative analgesic need (number of injections)</td>
<td>4.5 (0–23)</td>
<td>6.9 (0–49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Visual analogue pain score on postoperative day 1</td>
<td>4.6 (2.4)</td>
<td>5.4 (2.3)</td>
<td>0.003</td>
</tr>
<tr>
<td>Time first passing flatus (days)</td>
<td>2.4 (0–13)</td>
<td>3.1 (1–16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time of first bowel motion (days)</td>
<td>4.2 (2.0)</td>
<td>4.9 (2–15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to walk independently (days)</td>
<td>3.5 (0–14)</td>
<td>4.5 (1–14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>8.2 (2–99)</td>
<td>8.7 (3–39)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to resume household activity (days)</td>
<td>32.2 (4–365)</td>
<td>43.7 (7–198)</td>
<td>0.002</td>
</tr>
<tr>
<td>Distal margin (cm)</td>
<td>4.5 (3.0)</td>
<td>4.5 (2.7)</td>
<td>0.97</td>
</tr>
<tr>
<td>Lymph nodes removed</td>
<td>11.1 (7.9)</td>
<td>12.1 (7.1)</td>
<td>0.18</td>
</tr>
<tr>
<td>Direct cost (US$)</td>
<td>9297 (2091)</td>
<td>7148 (2164)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are mean (range) or mean (SD).

Table 2: Perioperative outcomes

Fr. Leung KL et al. Lancet 2004
Open vs Laparoscopic Rectal Surgery

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopic group (n=167)</th>
<th>Open resection group (n=170)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operative</td>
<td>38 (22.8%)</td>
<td>40 (23.5%)</td>
<td>0.97</td>
</tr>
<tr>
<td>Cancer related</td>
<td>1 (0.6%)</td>
<td>4 (2.4%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>26 (15.6%)</td>
<td>20 (11.8%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11 (6.6%)</td>
<td>16 (9.4%)</td>
<td></td>
</tr>
<tr>
<td>Probability of survival at 5 years*</td>
<td>76.1% (3.7%)</td>
<td>72.9% (4.0%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Recurrence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distant</td>
<td>37 (22.2%)</td>
<td>30 (17.6%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Local or peritoneal</td>
<td>11 (6.6%)</td>
<td>7 (4.1%)</td>
<td></td>
</tr>
<tr>
<td>Port site or wound (isolated)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Probability of disease free at 5 years*</td>
<td>75.3% (3.7%)</td>
<td>78.3% (3.7%)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

*Data are probability (SE).

Table 4: Survival and recurrence (stage I–III diseases)

Fr. Leung KL et al. Lancet 2004
Laparoscopic Rectal Surgery

• Laparoscopic surgery for rectal cancer appears to be oncologically similar to open surgery in the hands of experienced laparoscopic surgeons, but data are few

• Learning curve for laparoscopic TME is long, 40-80 cases

• Ongoing trials: COLORII (Eur), JCOG 0404 (Jpn), ACOSOG Z6051
Genetics and Colorectal Cancer

It is estimated that a third of patients with CRC have a familial component.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Gene</th>
<th>Lifetime CRC Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lynch</td>
<td><em>MLH1, MSH2, MSH6, PMS2</em></td>
<td>40-80%</td>
</tr>
<tr>
<td>Familial adenomatous polyposis (FAP)</td>
<td><em>APC</em></td>
<td>100% if unscreened</td>
</tr>
<tr>
<td>Juvenile polyposis</td>
<td><em>BMPR1A, SMAD4</em></td>
<td>9-68%</td>
</tr>
<tr>
<td>MYH-associated polyposis (MAP)</td>
<td>biallelic <em>MYH</em></td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td>monoallelic <em>MYH</em></td>
<td>8%</td>
</tr>
<tr>
<td>Peutz-Jeghers (PJS)</td>
<td><em>STK11</em></td>
<td>39-57%</td>
</tr>
<tr>
<td>Hereditary diffuse gastric cancer</td>
<td><em>CDH-1</em></td>
<td>Increased</td>
</tr>
<tr>
<td>PTEN hamartoma tumor</td>
<td><em>PTEN</em></td>
<td>Increased</td>
</tr>
<tr>
<td>Li-Fraumeni</td>
<td><em>p53</em></td>
<td>Increased</td>
</tr>
</tbody>
</table>

Fr. Raymond, 2009
<table>
<thead>
<tr>
<th>Condition</th>
<th>Associated Cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lynch</td>
<td>Brain (glioblastoma), endometrial, renal pelvis, sebaceous, small bowel</td>
</tr>
<tr>
<td>Familial adenomatous polyposis (FAP)</td>
<td>Brain (medulloblastoma, desmoid tumor, duodenal, hepatoblastoma, thyroid</td>
</tr>
<tr>
<td>Juvenile polyposis</td>
<td>Gastric, small bowel</td>
</tr>
<tr>
<td>MYH-associated polyposis (MAP)</td>
<td>Breast, pancreatic, small bowel</td>
</tr>
<tr>
<td>Peutz-Jeghers (PJS)</td>
<td>Breast, endometrial, male breast, renal, thyroid</td>
</tr>
<tr>
<td>Hereditary diffuse gastric cancer</td>
<td>Diffuse gastric (40-67% in men, 63-83% in women), lobular breast</td>
</tr>
<tr>
<td>PTEN hamartoma tumor</td>
<td>Breast, endometrial, male breast, renal, thyroid</td>
</tr>
<tr>
<td>Li-Fraumeni</td>
<td>Adrenocortical, brain, breast, leukemia, lymphoma, lung, sarcoma</td>
</tr>
</tbody>
</table>
FAP

• Autosomal dominant with high penetrance
• Usually presents by age 35
• Hundreds to thousands of polyps in colon
• CRC occurs in nearly 100% of carriers
• Accounts for 1% of CRC cases
• Almost monogenic - the result of mutations or deletions of the APC gene

Fr. Davidson NO. Keio J Med 2007
Lynch Syndrome (HNPCC)

• Autosomal dominant, associated with early onset of colon cancers, and with family history of colon, ovarian, endometrial, brain, small intestine, pancreatic, and urinary tract cancer

• Increased risk of CRC, and in female carriers, a 40-60% risk of endometrial cancer
Lynch Syndrome (HNPCC)

Bethesda Criteria

• CRC dx at < 50 yr
• or, w/ synchronous or metachronous CRC
• or, extracolonic cancer diagnosed at any age
• or, a first-degree relative with CRC diagnosed at < 50 yr or colorectal adenomas at < 40 yr
• or, CRC dx at < 60 yr with microsatellite instability (MSI)
Genetic Syndromes and CRC

• MSI (microsatellite instability) is increasingly being estimated in patients less than 60 years by Pathology
• Where patients meet criteria for syndromes, referral to Genetics and Genetic counselors should be offered
Summary

• Local recurrence rates for rectal cancer have significantly improved using TME and adjuvant radiotherapy or adjuvant radiochemotherapy

• Temporary diversion is indicated with low pelvic anastomoses after neoadjuvant radiotherapy or chemoradiotherapy

• Transanal resection for rectal cancer should be used very carefully and only for low risk T1N0 stage patients
Summary (2)

- Laparoscopic colectomy for colon cancer has similar oncologic results to open colectomy.
- Laparoscopic low anterior resection or laparoscopic-assisted APR is probably similar to open surgery for oncologic results, but data remain few – trials ongoing.
Summary (3)

• Increasing genetic information is available about inherited genetic syndromes related to CRC, and testing and counseling should be made available to patients likely to have such syndromes