SURGERY FOR COLORECTAL CANCER

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Abstract
Surgery is the mainstay in the treatment of colorectal cancer. Considerable progress has been made in the past eight years since the publication of the most recent clinical practice guidelines for colorectal cancer by the National Health and Medical Research Council. The most notable changes in surgery are the result of trials in minimally invasive approaches, including laparoscopic cancer resection, new advances yet to be tested such as robotic assisted cancer resection and the use of self-expanding metallic stents in patients with curable malignant obstruction. This paper provides an overview of these minimally invasive techniques and summarises the recommendations that could be considered for inclusion or update in the next edition of the guidelines.

Surgery is the mainstay treatment for colorectal cancer (CRC). With the exception of medically contraindicated patients or patients who decline surgery, most patients, including those with locally advanced or metastatic disease, will require some form of surgical intervention, which may be preceded by or followed by adjuvant therapy.

Although progress continues to be made on all fronts in the treatment of CRC, from a surgical standpoint, minimally invasive and maximally invasive resection techniques have made the most progress over the past eight years, since the publication of the most recent clinical practice guidelines by the National Health and Medical Research Council. Table 1 summarises the existing practice guidelines and areas where updates could be considered based on the available literature.

<table>
<thead>
<tr>
<th>Summary of 2005 NHMRC recommendations</th>
<th>Practice recommendation</th>
<th>Status</th>
<th>Considerations for updated recommendations based on current evidence – if applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>High ligation of the lymphovascular pedicle does not confer any oncological benefit. Resection where feasible should extend to the origin of the segmental vessels.</td>
<td>Equivocal</td>
<td>No change</td>
<td>For colon cancers, sharp fascial dissection with preservation of the mesocolon package and central vascular ligation requires further assessment.</td>
</tr>
<tr>
<td>The no-touch isolation technique has no oncological benefit.</td>
<td>Recommend</td>
<td>No change</td>
<td>N/A</td>
</tr>
<tr>
<td>Segmental resection is equivalent to extended resection in outcome.</td>
<td>Equivocal</td>
<td>No change</td>
<td>N/A</td>
</tr>
<tr>
<td>Sutured and stapled anastomosis have equivalent outcomes.</td>
<td>Strongly recommend</td>
<td>No change</td>
<td>N/A</td>
</tr>
<tr>
<td>Omental wrapping of anastomosis has no benefit.</td>
<td>Strongly not recommend</td>
<td>No change</td>
<td>N/A</td>
</tr>
<tr>
<td>Bilateral oophorectomy should be performed if there is obvious malignant disease of one or both ovaries.</td>
<td>Recommend</td>
<td>No change</td>
<td>N/A</td>
</tr>
<tr>
<td>Prophylactic bilateral oophorectomy for colon cancer cannot be supported by the available evidence.</td>
<td>Strongly not recommend</td>
<td>No change</td>
<td>N/A</td>
</tr>
<tr>
<td>In experienced hands, laparoscopic surgery for colon cancer has equivalent outcome to conventional surgery.</td>
<td>Recommend</td>
<td>No change</td>
<td>N/A</td>
</tr>
</tbody>
</table>
### FORUM

<table>
<thead>
<tr>
<th>Elective surgery for rectal cancer should be carried out by a surgeon who has undergone a period of special exposure to this form of surgery during surgical training, and who has maintained satisfactory experience in the surgical management of rectal cancer.</th>
<th>Recommend</th>
<th>No change</th>
<th>N/A</th>
</tr>
</thead>
</table>
| Local excision of T1 rectal cancer may be used in selected cancer patients according to the following guidelines:  
- mobile tumour < 3 cm  
- T1 on endorectal ultrasound  
- not poorly differentiated on histology (biopsy). | Equivocal | No change | N/A |
| A distal margin of 2 cm (fresh) is recommended in most instances, or 1 cm fixed. | Recommend | No change. Consideration for update | A 1 cm distal margin may be acceptable in selected patients.62,63 |
| Sphincter-saving operations are preferred to abdominoperineal resection except in the presence of:  
- tumours such that adequate distal clearance (> 2 cm) cannot be achieved  
- the sphincter mechanism is not adequate for continence  
- access to the pelvis makes restoration technically impossible (rare). | Equivocal | No change. Consideration for update | A 1 cm distal margin may be acceptable in selected patients to allow a restorative procedure. 62,63 |
| For mid-to-low rectal tumours, the principles of extra fascial dissection and total mesorectal excision (TME) are recommended. | Recommend | No change | N/A |
| Where technically feasible, the colonic reservoir is recommended for anastomosis within 2 cm from anorectal junction. | Strongly recommend | No change. Consideration for update | The use of coloplasty is an alternative to a colonic reservoir. |
| Routine drainage should only be considered for rectal cancers. | Equivocal | No change | N/A |
| N/A | N/A | Consideration for update | In experienced hands, laparoscopic rectal resection is safe and seems to have equivalent outcomes to open surgery. |
| N/A | N/A | Consideration for update | The use of robotic colorectal resection needs to be further assessed in prospective randomised trials. |
| Primary resection of obstructing carcinoma is recommended unless the patient is moribund. | Recommend | No change. Consideration for update | Routine use of self-expanding metallic stents as a bridge to surgery for curable obstructing cancer cannot be supported based on available evidence. |
| N/A | N/A | Consideration for update | Enhanced recovery programs should be considered in the care of colorectal patients undergoing elective resection. |

### Laparoscopic colon resection

Laparoscopic colectomy for cancer is a safe alternative to open surgery, provided the same surgical and oncological principles are adhered to. Short-term surgical outcomes such as intra-operative blood loss, post-operative pain, return of gastro-intestinal function and length of hospital stay, have all been consistently shown to improve, although only marginally, with laparoscopic surgery.2–5 However, the oncological outcomes of laparoscopic CRC resection remained a concern until more recently, when the long-term follow-up data from several large multi-centre randomised control trials (RCTs), such as the Australasian Laparoscopic Colon Cancer Study (ALCCaS trial), Clinical Outcomes of Surgical Therapy (COST), Colon Cancer Laparoscopic or Open Resection I (COLOR I), Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (CLASIC) and Barcelona trials became available. All confirmed the equivalence of laparoscopic assisted resections to open procedures in terms of long-
term oncological outcomes, with no confirmation of initial suggestions that laparoscopic colectomy may be associated with increased risk of port site metastases.6,9 These results have re-affirmed the previous guidelines that laparoscopic colon resection can be considered now with Level 1 evidence to be safe, however laparoscopic rectal cancer surgery should remain in the confines of prospective RCTs (see later).

The ALCCaS, COST and CLASSIC trials have published short-term data with only marginal improvements in subjective outcomes in the laparoscopic groups consistent with previous meta-analyses, however the longer term oncological outcomes are all equivalent. In 2008, Lacy et al published the long-term follow-up results from the Barcelona trial at a median follow-up of 95 months, where recurrence rates, overall mortality and cancer related mortality were 18% vs 28% (p>0.05), 36% vs 49% (p>0.05) and 16% vs 27% (p>0.05) respectively for laparoscopic and open arms.2 Although local recurrence rates and survival favoured the laparoscopic group, these did not reach statistical significance.3 Jayne et al reported the long-term follow-up data from the CLASSIC trial in 2007.15 Although comparable oncological outcomes have been demonstrated, early reports from the CLASSIC trial were somewhat alarming because of the high conversion rate (29%) and increased mortality, as well as morbidity, with open conversion.3 Much debate has stemmed from these and other trial results suggesting that if the conversion rates are lowered, then the benefit of the laparoscopic procedure will be increased. However, maintaining the intention to treat analyses and inherent bias of this post-hoc analysis cannot support this, widespread assumption. Several meta-analyses pooling data from the large Barcelona, COST, COLOR I, CLASSIC I and ALCCaS RCTs have confirmed that laparoscopic colectomy is at least oncologically equivalent to open surgery and can be reasonably offered as an alternative to the open procedure, and that this choice is based on surgeon and patient preferences.5,11,12

**Laparoscopic rectal resection**

More recently, laparoscopy has also been extended to treat rectal cancer. To date, multiple large case series, uncontrolled comparative studies and non-randomised controlled trials have demonstrated that laparoscopic rectal resection confers the same short-term surgical benefits as laparoscopic colectomy, and that laparoscopic proctectomy is associated with less blood loss, reduced post-operative pain, earlier return of gastrointestinal function and shorter duration of inpatient stay.13–16 As randomised trial confirmation of the long-term oncological data are currently lacking for laparoscopic proctectomy, there are concerns about its oncological safety, just as there were initial concerns about the oncologic safety of laparoscopic colectomy.

Rectal cancer outcomes are directly related to the quality of surgery, where local recurrence rates have been shown to halve after the surgeons are trained to perform high quality total mesorectal excision (TME).17 However, although local recurrence is a useful marker of surgical quality, it is at best an indirect marker of quality of surgery. Further, as local recurrence requires large numbers of patients with long-term follow-up, it limits its usefulness for immediate feedback or early recognition and implementation of strategies to improve surgical quality. The completeness of excision and integrity of the mesorectum of the resected rectal specimen is not only a surrogate for quality surgery, it has also been shown to correlate with oncological outcomes such as local recurrence.18,19 In a sub-study of the Dutch TME trial, Nagtegaal et al reported that an incomplete mesorectum is associated with an increased risk of overall recurrence (35.6% vs 21.5%) and local recurrence (15.0% vs 8.7%).18 Using the grading system described by Nagtegaal et al, Maleskar et al demonstrated stepwise incremental risk of local recurrence with progressive deterioration in the quality of TME, where the risks of local recurrence were 1.6%, 5.7% and 41% with a complete, near complete and incomplete mesorectum respectively. The importance of an intact mesorectum is currently being further assessed in the Australian Laparoscopic Cancer of the Rectum Trial (A La CaRT) trial, which is an Australasian multi-centre trial comparing laparoscopic and open rectal resection for cancer.20

A number of prospective randomised trials have either been completed or are currently ongoing to assess laparoscopic rectal resection.10,20–25 In the CLASSIC trial, patients undergoing laparoscopic rectal resection were twice as likely to have an involved circumferential margin as patients undergoing open rectal surgery, although interestingly, this did not translate to a local recurrence or survival difference at three years follow-up.3,10 Ng and Leung et al have published several studies comparing laparoscopic and open rectal resection, including a 10 year follow-up study which showed that there was no difference in survival between the two groups (overall survival 83.5% vs 78% p>0.05, disease free survival 82.9% vs 80.4% p>0.05).21–22 Ongoing trials include the Comparison of Open versus laparoscopic surgery for mid and low REctal cancer After Neoadjuvant chemoradiotherapy (COREAN) trial from South Korea, COLOR II trial from Europe, the Australian Laparoscopic Cancer of the Rectum Trial (A La Cart) trial from Australia, and the Laparoscopic-Assisted or open resection rectal cancer trial from the United States.20,23–25 The first two trials have completed recruitment and are due to complete their three year follow-up by the end of 2013, while the latter two trials are still currently recruiting.23,24 Interim reports from the former two trials found no differences in lymph node yield, macroscopic quality of the TME or involvement of circumferential resection margin between laparoscopic and open surgery, thereby providing some evidence that laparoscopic surgery may be oncologically equivalent to open surgery.23,24 However, long-term follow up data are still required before definitive conclusions can be drawn.

**Robotic colorectal surgery**

Laparoscopic TME is a technically challenging procedure which can be made even more challenging in the setting of neoadjuvant chemoradiation, a narrow male pelvis or obesity. Improving surgical access within the confines of a bony pelvis may therefore improve the quality of TME while minimising inadvertent pelvic nerve injury, thus improving cancer outcomes as well as urinary and sexual
function.26 Robotic assisted surgery has the potential to mitigate some of the limitations of laparoscopy through its stable operating platform, improved depth perception and enhanced dexterity, while offering improved ergonomics for the surgeon to minimise fatigue. However, availability and costs hamper widespread dissemination of the technique.

Although robotic surgery is increasingly utilised in pelvic surgery, the collective international experience remains in its infancy. As far as the authors are aware, only one small RCT has been published to date comparing outcomes between robotic and laparoscopic total mesorectal excision, although a number of multi-centre randomised trials are currently underway to assess the safety and efficacy of robotic surgery for rectal cancer.27,28 Several large series and at least two systematic reviews have been published which suggest that robotic surgery is safe and that it is associated with less open conversion, with no differences in surgical morbidity, length of hospital stay and rates of involved margin.29-31 Promising as it is, until more data becomes available, there is insufficient evidence from a functional or oncological outcome perspective to justify the additional costs of robotic surgery.

Self-expanding metallic stents for CRC

The use of self-expanding metallic stents for obstructing CRC as definitive treatment in a palliative setting is well established.32,33 As experience with self-expanding metallic stents grows, its indications have also expanded to include curable obstructing CRC as a bridge to elective surgery. This approach is attractive because not only does it reduce the morbidity associated with an emergency resection, it also permits bowel preparation and pre-operative colonoscopic assessment of the proximal colon, the use of laparoscopic resection while minimising the likelihood of requiring a stoma. However, the use of self-expanding metallic stents as a bridge to surgery is also contentious because of the potential for tumour dissemination from stent related perforation, which may convert a curable CRC into an incurable cancer.

Although self-expanding metallic stents have been assessed in numerous studies, few of these studies are prospective randomised trials.34,35 Further, while the short-term safety of self-expanding metallic stents has been established, the same cannot be said about the oncological safety of self-expanding metallic stents as a bridge to surgery, because most studies do not report long-term outcomes.36 Studies by Said et al, Dastur et al and Kavanagh et al did not reveal any differences in survival, but alarmingly, in a recent publication by Sabbagh et al, five year overall survival and cancer related mortality were both worse in the self-expanding metallic stents group compared to the group that underwent surgical decompression.36-38 Further, five year disease free survival and time to recurrence also tended to favour the surgical decompression group. Although this was not statistically significant, it might have been related to the small sample size in that study.37 More long-term follow-up data are required to determine the safety of self-expanding metallic stents as a bridge to surgery in patients with curable CRC.

Pelvic exenteration for locally advanced and recurrent rectal cancer

Since the last guidelines, numerous international and national publications have confirmed the safety and survival advantage of pelvic exenteration for recurrent rectal cancer.40-42 Provided a clear microscopic resection margin can be achieved, five year overall survival of 30-50% have been reported.40 With improved surgical techniques and experience with extra-anatomical dissection, local recurrences in challenging anatomical locations such as the pelvic side wall, recurrences involving proximal sacral segments or pubic bone are increasingly being offered curative surgery.43,44 Specialised units with an interest in maximally invasive surgery have also pushed the boundary of resectability further by offering pelvic exenteration in patients with isolated resectable metastasis of the liver or lung. Although morbidity of pelvic exenteration remains high, long-term oncological benefit of pelvic exenteration coupled with good quality of life outcomes have cemented the role of pelvic exenteration for locally recurrent rectal cancer.45

Role of local excision for rectal cancer

Transanal excision of rectal cancers has traditionally been reserved for old and medically frail patients who are unable to tolerate a major resection. However, in selected rectal cancers, namely early rectal cancers (T1 cancers) with no adverse features on histology, patients may be spared the morbidity of a major resection or a permanent colostomy without compromising oncological outcomes.46,47 The major disadvantage with the conventional local excision technique though, is the quality and completeness of resection, as well as access difficulties which limit the applicability of the technique to the low rectum. With the advent of transanal endoscopic microsurgery, the incidence of surgical site recurrence has reduced and the quality of the specimen improved.48 Although the risk of loco-regional recurrence from unrecognised nodal involvement remains, the risk of this is low provided case selection is appropriate.49 Unfortunately, because of the limitations of existing staging modalities and our understanding of tumour biology, some cancers will recur despite seemingly appropriate case selection. Outcome of surgical salvage in the event of local recurrence is variable and further highlights the importance of accurate staging of the primary and appropriate case selection. To minimise the risk of local recurrence, selected centres are offering neoadjuvant chemoradiotherapy as an adjunct to local excision.50,51 However, the safety and morbidity of this approach remains under-studied and needs further evaluation before it can be recommended.

Care of the post-operative patient

The principle of enhanced recovery after surgery, also known as fast track surgery, is to minimise surgical trauma thereby reducing ileus and post-operative pain.52 In doing so, time to resumption of diet, surgical morbidity and length of stay in hospital have all been proven to reduce.53-55 Although initially described for elective open colectomy, the principles of enhanced recovery programs are also increasingly applied to laparoscopic procedures and rectal surgery with similar benefits.56,57
Conclusions

Considerable progress has been made in the surgical treatment of CRC. Notable changes relate to minimally and maximally invasive approaches to cancer resection, as well as care of the post-operative surgical patient. Inclusion of these developments in the next edition of CRC practice guidelines should be considered.

References

ColonoScopy and colorectal canCer

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Abstract

ColonoScopy has a central role in the detection and prevention of colorectal cancer. This is based on the fact that most colorectal cancer develops from premalignant adenomatous or serrated polyps, which can be removed at colonoscopy and hence prevent the development of colorectal cancer. The success of colonoscopy in preventing bowel cancer is dependent on the quality of the colonoscopy performed. This review highlights the key performance indicators measuring quality of colonoscopy, including consent, indication, preparation, caecal intubation rates, polyp detection and removal, withdrawal time and complication rates, and sets minimum target recommendations for each of the key performance indicators.

Does colonoscopy prevent colorectal cancer?

The evidence for colonoscopy reducing the incidence of colorectal cancer (CRC) comes mostly via indirect evidence from a number of observational, cohort studies. While the National Polyp Study demonstrated a risk reduction in the development of CRC of 76 per cent to 90 per cent post polypectomy, other studies have shown a more modest risk reduction. In addition, more recent evidence suggests that in real world community practice, colonoscopy affords a greater level of protection against the development of cancers on the left side of the colon than the right side. The reason for this is not entirely clear, but could include patient factors (bowel prep and tumour biology), colonoscopist factors (technique, knowledge, personality and perceptual factors), system drivers and equipment factors. The more aggressive biology of right sided cancer might be a factor and a recent study has confirmed that a higher proportion of right sided cancers after recent colonoscopy are microsatellite unstable. However, low polypectomy rates and a high proportion of incomplete colonoscopies seem a common theme in many