Developments in early rectal cancer treatment

Simon P. Bach

Academic Department of Surgery, Queen Elizabeth Hospital, Edgbaston, Birmingham, UK

Bowel cancer screening will change how rectal cancer presents. Data from the two UK pilots has shown that 49–62% of screen-detected tumours are 'early' (pT1–2N0M0; Stage I) [1,2]. Radical total mesorectal excision (TME) offers high rates of cure for early rectal cancer; only 3–6% of patients subsequently relapse [3–5]. There are concerns, however, that radical surgery, which evolved to treat locally advanced, symptomatic tumours, may not be the optimal method of treatment for early (screen detected) tumours.

TME surgery is associated with iatrogenic effects such as pain, infection, incontinence, impotence and occasionally death. Six-month mortality following radical curative surgery for rectal cancer is 4.6% for patients aged 65–74 years and 13.4% for patients aged 75–84 years according to the Netherlands registry and RCT data collated since 1990 [6]. The Dutch TME trial reported clinical bowel leaks in 16% of non-irradiated subjects [7]. Pelvic dissection may cause autonomic nerve damage despite the advent of nerve sparing techniques, leading to urinary (25–34%) and sexual dysfunction [8,9]. More than half of all patients experience some form of faecal incontinence following TME, and 30–40% suffer daily symptoms of urgency, incomplete emptying and stool frequency [9, 10]. Three prospective cohort studies have examined health related quality of life scores following rectal cancer surgery [11–13]. Each demonstrated persistently poor social, role, body image and defaecation scores.

The question remains whether this level of surgical morbidity and mortality is necessary for the satisfactory treatment of early rectal cancer? Local treatment, with radical therapy salvage in the event of recurrence, could be safer and functionally far superior without substantially compromising cancer survival. We believe that the literature supports use of downstaging radiotherapy and local excision as an alternative to radical surgery for curative treatment of selected rectal cancers.

Local excision alone may be curative for the majority of early tumours; however, recurrence rates of 10–30% amongst higher risk lesions are unacceptable [14]. There is currently no means to precisely identify cases that later recur following local excision. Selective post-operative radiotherapy for all tumours with less favourable histopathological characteristics does not produce satisfactory outcomes [14,15].

It seems probable that a strategy of organ preservation using downstaging radiotherapy with a long interval to transanal endoscopic microsurgery (TEMS) may produce substantial benefits in terms of reduced morbidity and mortality with long lasting improvements in quality of life. Due to low toxicity, short course pre-operative radiotherapy (SCPRT) is an attractive treatment choice for these early tumours [16,17]. Preliminary data suggest high rates of downstaging following SCPRT if surgery is delayed, in both early and advanced disease [17,18].

While this strategy would not be expected to produce an oncological improvement over radical surgery, widespread benefits are likely to outweigh a small increased risk of recurrence. Limited literature using pre-operative radiation with a long interval to local excision for T1 and T2 tumours would suggest that recurrence rates are low [17,19,20]. Indeed recurrence rates following organ preservation may be no higher than the combined rate of perioperative mortality and recurrence in radically treated subjects. Further improvements in surveillance following local treatment will optimise successful radical therapy salvage.

The TREC study (Transanal endoscopic microsurgery and Radiotherapy in Early rectal Cancer) is a randomised late phase II trial for T1–2N0M0 rectal cancer defined according to MRI and ERUS. It will compare radical TME surgery (current gold standard) versus SCPRT and delayed local excision using TEMS at 8–10 weeks. This feasibility study will assess recruitment and provide estimates of safety/efficacy in order to refine the design of a large, multicentre phase III trial.

Conflict of interest statement

None declared.

References

1 UK Flexible Sigmoidoscopy Screening Trial Investigators. Single flexible sigmoidoscopy screening to prevent colorectal cancer: baseline findings of a UK multicentre randomised trial. *Lancet* 2002;**359**(9314):1291–300.

2 UK Colorectal Cancer Screening Pilot Group. Results of the first round of a demonstration pilot of screening for colorectal cancer in the United Kingdom. *BMJ* 2004;**329**(7458):133.

3 Bentrem DJ, Okabe S, Wong WD, et al. T1 adenocarcinoma of the rectum: transanal excision or radical surgery? *Ann Surg* 2005;**242**(4):472–7.

4 Endreseth BH, Myrvold HE, Romundstad P, Hestvik UE, Bjerkeset T, Wibe A. Transanal excision vs. major surgery for T1 rectal cancer. *Dis Colon Rectum* 2005;**48**(7):1380–8.

5 Peeters KC, Marijnen CA, Nagtegaal ID, et al. 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. *Ann Surg* 2007;**246**(5):693–701.

6 Rutten HJ, den Dulk M, Lemmens VE, van de Velde CJ, Marijnen CA. Controversies of total mesorectal excision for rectal cancer in elderly patients. *Lancet Oncol* 2008;**9**(5):494–501.

7 Marijnen CAM, Kapiteijn E, van de Velde CJH, et al.; Cooperative Investigators of the Dutch Colorectal Cancer Group. Acute side effects and complications after short-term preoperative radiotherapy combined with total mesorectal excision in primary rectal cancer: report of a multicenter randomized trial. *J Clin Oncol* 2002;**20**(3):817–25.

8 Hendren SK, O'Connor BI, Liu M, et al. Prevalence of male and female sexual dysfunction is high following surgery for rectal cancer. *Ann Surg* 2005;**242**(2):212–23.

9 Wallner C, Lange MM, Bonsing BA, et al. Causes of fecal and urinary incontinence after total mesorectal excision for rectal cancer based on cadaveric surgery: A study from the cooperative clinical investigators of the Dutch Total Mesorectal Excision trial. *J Clin Oncol* 2008;**26**(27):4466–72.

10 Temple LK, Bacik J, Savatta SG, et al. The development of a validated instrument to evaluate bowel function after sphincter-preserving surgery for rectal cancer. *Dis Colon Rectum* 2005; **48**(7):1353–65.

11 Engel J, Kerr J, Schlesinger-Raab A, Eckel R, Sauer H, Holzel D. Quality of life in rectal cancer patients: a four-year prospective study. *Ann Surg* 2003;**238**(2):203–13.

12 Grumann MM, Noack EM, Hoffmann IA, Schlag PM. Comparison of quality of life in patients undergoing abdominoperineal extirpation or anterior resection for rectal cancer. *Ann Surg* 2001;**233**(2):149–56.

13 Wilson TR, Alexander DJ. Clinical and non-clinical factors influencing postoperative health-related quality of life in patients with colorectal cancer. *Br J Surg* 2008;**95**(11):1408–15.

14 Bach SP, Hill J, Monson JR, et al. A predictive model for local recurrence after transanal endoscopic microsurgery for rectal cancer. *Br J Surg* 2009;**96**(3):280–90.

15 Greenberg JA, Shibata D, Herndon JE, Steele GD, Mayer R, Bleday R. Local excision of distal rectal cancer: an update of cancer and leukemia group B 8984. *Dis Colon Rectum* 2008; **51**(8):1185–91.

16 Bujko K, Nowacki MP, Nasierowska-Guttmejer A, Michalski W, Bebenek M, Kryj M. Long-term results of a randomized trial comparing preoperative short-course radiotherapy with preoperative conventionally fractionated chemoradiation for rectal cancer. *Br J Surg* 2006;**93**(10):1215–23.

17 Bujko K, Richter P, Kolodziejczyk M, et al. Preoperative radiotherapy and local excision of rectal cancer with immediate radical re-operation for poor responders. *Radiother Oncol* 2009.

18 Radu C, Berglund K, Påhlman L, Glimelius B. Short-course preoperative radiotherapy with delayed surgery in rectal cancer – a retrospective study. *Radiother Oncol* 2008;**87**(3):343–9.

19 Lezoche E, Guerrieri M, Paganini AM, Baldarelli M, De Sanctis A, Lezoche G. Long-term results in patients with T2–3 N0 distal rectal cancer undergoing radiotherapy before transanal endoscopic microsurgery. *Br J Surg* 2005;**92**(12):1546–52.

20 Borschitz T, Wachtlin D, Möhler M, Schmidberger H, Junginger T. Neoadjuvant chemoradiation and local excision for T2–3 rectal cancer. *Ann Surg Oncol* 2008;**15**(3):712–20.