

Canadian Association of General Surgeons, the American College of Surgeons, the Canadian Society of Colorectal Surgeons, and The American Society of Colon and Rectal Surgeons: Evidence-Based Reviews in Surgery – Colorectal Surgery

Carl Brown, M.D., • Julio Garcia-Aguilar, M.D., • P. Terry Phang, M.D.,
for the members of the Evidence-Based Reviews in Surgery Group

The term “evidence-based medicine” was first coined by Sackett and colleagues as “the conscientious, explicit and judicious use of the current best evidence in making decisions about the care of individual patients.”¹ The key to practicing evidence-based medicine is applying the best current knowledge to decisions in individual patients. Medical knowledge is continually and rapidly expanding and reading all of the medical literature is impossible for an individual clinician. For clinicians to practice evidence-based medicine, they must have the skills to read and interpret the medical literature so they can determine the validity, reliability, credibility, and utility of individual articles, *i.e.*, critical appraisal skills. Generally, critical appraisal requires that the clinician have some knowledge of biostatistics, clinical epidemiology, decision analysis, and economics as well as clinical knowledge.

The Canadian Association of General Surgeons and the American College of Surgeons jointly sponsored a program entitled “Evidence-Based Reviews in Surgery (EBRS),” supported by an educational grant from Ethicon, Inc. and Ethicon Endo Surgery, Inc. and Ethicon Endo Surgery. The primary objective of this initiative is to help practicing surgeons improve their critical appraisal skills. Beginning in 2007; EBRS also included a module covering topics in colorectal surgery. Each academic year, six clinical articles are chosen for review and discussion. The articles are selected not only for their clinical relevance to colorectal surgery but also to cover a spectrum of methodologic issues important to surgeons; for example, causation or risk factors for disease, natural history or prog-

nosis of disease, quantifying disease (measurement issues), diagnostic tests and the diagnosis of disease, and the effectiveness of treatment. Both methodologic and clinical reviews of the article are performed by experts in the relevant areas and posted on the EBRS-CRS website. As well, a listserv discussion will be held where participants can discuss the monthly article. Members of Canadian Association of General Surgeons (CAGS) and the American College of Surgeons (ACS) can access Evidence-Based Reviews in Surgery–Colorectal through the Canadian Association of General Surgeons website (www.cags-accg), the American College of Surgeons website (www.facs.org), the Canadian Society of Colon and Rectal Surgeons (CSCRS) website (www.cscrs.ca), and the American Society of Colon and Rectal Surgeons (ASCRS) website (www.fascrs.org). All journal articles and reviews are available electronically through the website. Surgeons who participate in the current (modules) packages can receive CME and/or Maintenance of Certification credits by completing an evaluation and a series of multiple choice questions. For further information about EBRS-CRS readers are directed to the CAGS, ACS, CSCRS, and ASCRS websites or should email the administrator, Marg McKenzie at mmckenzie@mtsinai.on.ca.

In addition to making the reviews available through the CAGS and the ACS websites, a condensed version of the reviews will be published in *Diseases of the Colon and Rectum*. This month’s article by the Mercury Study Group “Diagnostic accuracy of preoperative magnetic resonance imaging in predicting curative resection of rectal cancer”² is the first in the series for DCR. We hope readers will find EBRS useful in improving their critical appraisal skills and also keeping abreast of new developments in general surgery. Comments about EBRS may be directed to Marg McKenzie at mmckenzie@mtsinai.on.ca.

Dis Colon Rectum 2009; 52: 1–3
DOI: 10.1007/DCR.0b013e31819796ff
©The ASCRS 2009

SELECTED ARTICLE

MERCURY Study Group. Diagnostic Accuracy of Preoperative Magnetic Resonance Imaging in Predicting Curative Resection of Rectal Cancer: Prospective Observational Study. *BMJ* 2006;333(7572):779–84.

QUESTION: Is magnetic resonance imaging (MRI) accurate in predicting surgical resectability of rectal cancer with circumferential resection margins (CRM) at least 1 mm clear of tumor invasion?

DESIGN: Prospective observational study.

SETTING: Eleven colorectal surgery units in four European countries.

PATIENTS: Of the 679 patients consented, complete pathology and MRI were available on 408 patients.

TEST AND DIAGNOSTIC STANDARD: All patients underwent MRI of the pelvis with a body coil and high resolution protocol for imaging of the primary tumor and mesorectal fascia before surgery.

MAIN OUTCOME: Accuracy of MRI in predicting a curative resection based on the histologic yardstick of presence or absence of tumor at the margins of the specimen.

RESULTS: High resolution scans were technically satisfactory in 93 percent (379 of 408 patients). Surgical specimens were histopathologically graded as complete or moderate in 80 percent (328 of 408 patients) and the median lymph node harvest was 12 nodes (range, 0–49). Three hundred and fifty-four patients had negative CRM of which 327 cases were predicted by the MRI (specificity, 92 percent; 95 percent, CI 90 to 95 percent). Fifty four patients had positive CRM of which 32 cases were predicted by MRI (sensitivity, 59 percent; 95 percent, CI 46 to 72 percent). The likelihood ratio for a positive test was 7.77 and the likelihood ratio for a negative test was 0.44.

CONCLUSIONS: MRI of rectal cancer is accurate, feasible, reproducible, and a standard for preoperative staging.

COMMENTARY: The proximity of rectal cancer to within 1 mm of the fascia propria and the true radial margin in the surgical specimen strongly predict recurrence and survival in patients undergoing radical surgery. Preoperative knowledge of the relationship of the tumor to the fascia propria of the rectum is important for decisions about the optimal treatment plan including the use of neoadjuvant chemoradiation and the extent of surgery.

The study conducted by the Mercury Study Group was a landmark in the field of rectal cancer as the first prospective multi-institutional study to assess the accuracy of MRI in predicting curative resection in patients with rectal cancer. Between January 2002 and October 2003, 679 consecutive patients with rectal cancer treated at 11 different hospitals were evaluated for participation in the study. After application of exclusion criteria, 408 patients were included. While exclusion of over one-third of eligible patients raises concerns regarding the validity of the conclusions, the authors account for all of the

exclusions and most of the patients excluded did not undergo surgical removal of the tumor ($n = 146$) for various reasons. Furthermore, the age, gender, and T stage of patients in this study were similar to recent population-based data on patients with rectal cancer, suggesting reasonable external validity.

Included patients had preoperative MRI interpreted by an experienced radiologist who reported on the status of the tumor in relation to the *fascia propria* of the rectum with a margin ≤ 1 mm considered to be potentially affected. After surgical resection, specialist gastrointestinal pathologists assessed the surgical specimen for circumferential resection margin (CRM); a positive CRM was defined by tumor within 1 mm of the *surgical* resection margin. Most patients received an attempted curative resection, with or without preoperative short-course radiotherapy. Patients with suspected locally advanced rectal cancer ($n = 97$) received changes in their treatment strategies designed to either reduce the tumor volume, *i.e.*, preoperative chemoradiotherapy, or received a more extensive surgical resection, *e.g.*, multivisceral resection. To mitigate the impact of neoadjuvant therapy on the assessment of MRI as a diagnostic tool, the latter patients were reassessed with a posttreatment preoperative MRI. However, 22 of these patients did not receive the second MRI evaluation and were excluded from the study. The remaining patients who underwent posttreatment MRI accounted for 21 of the 27 patients with false positive MRI evaluations. The authors speculate that radiation-related fibrosis may have given the false appearance of tumor at the margins. Thus, the inclusion of these patients in this study resulted in a reduction in the reported accuracy of MRI.

While the impact of the MRI results on the surgical approach in these patients was difficult to measure, surgeons who were aware of preoperative MRI suggesting close radial margins would be more likely to err on the side of wider resection margins. These clinical judgments would presumably bias the results toward lower accuracy in these patients, as a more aggressive surgical approach could lead to fewer positive margins than predicted by MRI. However this pragmatic approach for resection margins mimics usual clinical practice.

Overall, the sensitivity of MRI for predicting involved circumferential surgical resection margins was 59 percent (32/54) and the specificity was 92 percent (327/354) and the accuracy was 85 percent. The calculated likelihood ratio of an involved circumferential margin (CRM) on preoperative MRI is 7.7; this ratio implies that the likelihood of a positive CRM increased almost eightfold if MRI is positive and a negative MRI result decreased the likelihood by approximately 50 percent. In tethered/fixed tumors treated using preoperative chemoradiation, the accuracy of MRI decreased to 77 percent but the negative predictive value remained high at 98 percent. Decreased

accuracy in the preoperative chemoradiation group was because of a high false positive rate; this increased false positive rate likely attributed to residual bulk but the absence of cancer as the tumor shrinks away from the margins.

The importance of the scanning technique in MRI assessment of rectal cancer and standardization of interpretation and reporting cannot be overemphasized. In this study, participating radiologists held workshops to ensure consistency in scanning technique. The reproducibility of the MERCURY study results will require adherence to the imaging sequences and reporting described in the manuscript appendix. Similarly, participating pathologists held prestudy workshops to ensure consistency of assessment and reporting of operative specimens and all surgeons participated in workshops to learn total mesorectal excision. Consequently to generalize the results of this study, the quality of the surgical procedure (a total mesorectal excision) and pathologic evaluation of the surgical specimen (including whole mount sections) must be standardized. Radiologists, surgeons, and pathologists participating in the study were all part of multidisciplinary teams committed to improving the quality of imaging, surgery, and pathology in rectal cancer.

Currently, imaging of rectal lesions with endorectal ultrasound (ERUS) is performed routinely at many centers as an alternative to MRI for local staging. ERUS provides excellent images of the different layers of the rectal wall and is more accurate in staging tumors that are

limited to the rectal wall or may be superficially invading the mesorectum. ERUS is useful in identifying T1 or T2 (NO) lesions where benefits of preoperative radiotherapy appear to be lacking. On the other hand this study does confirm the utility of MRI in distinguishing patients at risk for locally invasive disease (*i.e.*, positive circumferential margins), who may benefit from preoperative chemoradiation where ERUS is still useful in suspected T1 or T2 (NO) lesions where preoperative therapy would not be beneficial and is associated with adverse outcomes.

In summary, the MERCURY study confirmed that MRI can accurately predict involved circumferential radial margins in patients with advanced rectal cancer. The selective use of ERUS or MRI based on clinical impression of the depth of invasion and tumor height appears to be the most rational approach to imaging patients with rectal cancer for treatment and operative planning. These imaging techniques should be considered complementary rather than mutually exclusive.

REFERENCES

1. Anonymous. Evidence-based medicine. Evidence Based Medicine Working Group. JAMA 1992;268:2420–5.
2. MERCURY Study Group. Diagnostic accuracy of preoperative magnetic resonance imaging in predicting curative resection of rectal cancer: prospective observational study. BMJ 2006;333:779–84.