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Colorectal Cancer Guideline Reflects International Practice Variations

By: Anne Lin, MD, FACS, FASCRS and Clifford Ko, MD, MS, MSHS, FACS, FASCRS

In November of 2011, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom (UK) updated their clinical guideline: Colorectal cancer. The diagnosis and management of colorectal cancer. (1) The update offers guidance on a wide variety of issues, including diagnostic investigation and staging of colorectal cancer, use of neo-adjuvant radiation or chemoradiotherapy, management of locally excised stage I colorectal cancer, sequence of chemotherapy for advanced and metastatic colorectal cancer, and follow-up surveillance after curative resection.

An important part of treatment of rectal cancer relies on the ability to stage, or accurately and consistently identify, the appropriate subset of patients who should undergo neo-adjuvant therapy. Given the toxicity of radiation therapy, achieving minimal chance of local recurrence without overtreatment is one of the key principles to successful treatment of rectal cancer. Notable differences between the NICE guideline recommendations when compared with guidelines developed in the United States (US), such as the 2012 National Comprehensive Cancer Network (NCCN), include choice of imaging modality, predictions of local recurrence, and neo-adjuvant treatment. (2) These differences reflect variations in the practice philosophies of clinicians in the United Kingdom and their US colleagues.

One notable difference between the NICE and NCCN guidelines is the use of ultrasound versus magnetic resonance imaging (MRI) for rectal cancer staging. MRI appears to be the modality of choice for staging rectal cancers in the UK, and is used to determine the increased risk of local recurrence based on anticipated circumferential resection margin (outer radial margin tumor extension), and lymph node enlargement (presumably due to tumor burden). In the US, however, ultrasound is used frequently as a staging modality and has advantages for discerning early T1 and T2 tumors.

good prognostic patients for total mesorectal excision (TME) surgery alone. (5) Good prognostic features included >1 mm CRM, and <5 mm T3 extension. Poor prognostic features included CRM that was <1 mm or involved, deeper cT3 extension (>5 mm) or cT4, intersphincteric plane involved by tumor, and positive extramural venous invasion. The study showed that MRI could be used to accurately select good prognostic rectal cancer patients and that rates of disease free survival and local recurrence were comparable to other studies with TME alone. Nodal stage, however, was not used to determine good or poor prognosis subgroups in this study. Thus, one must keep in mind that the low observed local recurrence rates noted in the study may be due to the policy of treating node positive patients with single agent fluoropyrimidine-based chemotherapy.

With regards to prediction of lymph nodes, Guillem et al. questioned the accuracy of using endorectal ultrasound or MRI for predicting mesorectal lymph node involvement in a cT3, N0 cohort. (6) Despite neo-adjuvant combined modality treatment (CMT), 22% of patients were noted to have residual positive lymph nodes on resection specimen. The study warned against under-treatment of ultrasound or MRI-staged T3N0 patients given the limited ability to accurately assess for positive lymph nodes.

A second notable difference between the NICE and US-based guidelines, such as those from NCCN, is the indication for which patients should undergo neo-adjuvant therapy. NICE recommends radiation and chemotherapy using MRI predictions of low, moderate, or high risk for local recurrence of rectal cancer as shown in the table below.

Table 1: Risk of Local Recurrence for Rectal Tumours as Predicted by MRI*

Risk of Local Recurrence	Characteristics of Rectal Tumours Predicted by MRI
High	• A threatened (<1 mm) or breached resection margin **or** • Low tumours encroaching onto the inter-sphincteric plane **or** with levator involvement

Moderate	• Any cT3b (1-5 mm) or greater (>5 mm), in which the potential surgical margin is not threatened **or** • Any suspicious lymph node not threatening the surgical resection margin **or** • The presence of extramural vascular invasion (2)
Low	• cT1 or cT2 or cT3a (<1 mm) **and** • No lymph node involvement

* Modified from National Institute for Health and Clinical Excellence. Colorectal cancer. The diagnosis and management of colorectal cancer. London: National Institute for Health and Clinical Excellence; 2011. 31 p.

The NICE guideline does not recommend neo-adjuvant treatment for low-risk operable rectal cancer, unless as part of a clinical trial, while reserving neo-adjuvant therapy (short-course radiotherapy or chemoradiation) for the moderate- or high-risk subgroups, respectively. In contrast, the NCCN guideline recommends neo-adjuvant chemoradiation therapy for patients based on the American Joint Committee on Cancer staging principles, specifically, for those patients with cT3, N0 or any T, N1-2 rectal cancer.

The third notable difference between UK and US practice surrounds the use of neo-adjuvant radiation therapy, specifically short-course versus long-course therapy. The use of short-course radiation is part of the neo-adjuvant armamentarium in Europe. In comparison, short course radiation is more limited in use in the US. Since the National Institutes of Health (NIH) consensus statement was released in 1990, the standard of care in the US has been to give CMT (chemoradiation followed by surgery) for advanced stage rectal cancer. (7) While certain debates such as timing of chemoradiation (neo-adjuvant versus adjuvant) have been largely settled, type of CMT (short-course radiation versus standard long course of chemoradiation) has not been uniformly agreed upon in the US. Regardless of length of radiation treatment, one overarching important principle for reducing local recurrence rate is proper education and training on the technique of TME to achieve a negative CRM. (8-10)

In summary, the different practices noted between the British and US guidelines are related to the primary use of MRI for staging in the UK, which allows for better delineation of the heterogeneous cT3 subgroups. The NICE guidelines take into account the improved prognosis of patients with cT3a tumors and limits neo-adjuvant treatment to patients with moderate- or high-risk T3 rectal cancer given that the benefits of neo-adjuvant treatment are presumably limited for low-risk cT3a tumors if TME with complete CRM can be performed. A

Authors

Anne Lin, MD, FACS, FASCRS
UCLA Department of Surgery
David Geffen School of Medicine at UCLA
Los Angeles, California

Clifford Y Ko, MD, MS, MSHS, FACS, FASCRS
UCLA Department of Surgery
David Geffen School of Medicine at UCLA
Los Angeles, California

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Potential Conflicts of Interest

Dr. Lin and Dr. Ko state no financial or personal conflicts of interest with respect to this commentary.

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