

Colorectal cancer—moving forward one step at a time

Introduction

Colorectal cancer remains a disease with urgent need for improved outcomes. It is the third most common malignancy worldwide, representing not only 10% of all cancer diagnoses, but the second commonest cause of cancer deaths (1). Despite some improvements over recent decades, relapse rates for locally advanced disease remain high and survival of metastatic disease remains modest.

The largest improvements in overall survival can be gained by prevention of relapse of early stage disease and thus increasing the number of patients who survive long term. However despite the wide adoption of neoadjuvant chemoradiation (for rectal cancer) and adjuvant systemic therapy, there has been little or no impact on the poor survival outcomes for locally advanced disease.

The many attempts to trial new agents for systemic therapy have unfortunately been largely unsuccessful. The mainstay of systemic treatment remains fluoropyrimidine chemotherapy combined with oxaliplatin in the adjuvant setting, established in 2009 by the MOSAIC trial (2), and associated with a 10-year overall survival in stage II and III disease of only 71.7% (3).

Pending discovery and development of more efficacious systemic agents, there is room to optimize, improve and repurpose currently available diagnostic and therapeutic technologies. This special edition focusses on areas of highest need, where treatment optimisation may translate into better outcomes for patients with colorectal cancer.

Imaging

Diagnostic imaging is the mainstay of preoperative cancer staging and essential to inform a multidisciplinary treatment plan. In the rectal cancer setting, this is already very well established. As Dr Hui and colleagues discuss in this edition, both high quality images and high quality synoptic reporting are essential for the best outcomes for patients (4). Synoptic reports contain more detail with attention to characteristics of the tumor important for multidisciplinary decision making. The skill of the reporting radiologist is critical, and despite promise, has not yet been superseded by Artificial Intelligence

With the increasing interest in broadening the use of neoadjuvant therapy into colonic cancers, diagnostic imaging will play an increasing role in preoperative staging of these cancers. There remains significant room for innovation and improvement, with inaccuracy of current staging methods being a major limitation of ongoing neoadjuvant chemotherapy trials.

Systemic therapy

The development of systemic treatments for early colorectal cancer can be summed up in just a few sentences. Adjuvant chemotherapy was shown to have a survival benefit in the early 1990s with fluoropyrimidine based therapy (5-8). Subsequently, in 2009, oxaliplatin was shown to add to this benefit with a further improvement in overall survival (2).

There are some notable failures worth mentioning, with cetuximab (an EGFR antibody) (9), bevacizumab (a VEGF antibody) (10) and irinotecan (a topoisomerase inhibitor) (11), none of which showed survival benefit used adjuvantly despite benefit in the metastatic setting.

Given the lack of effective systemic agents for eradication of micrometastatic disease, the optimal sequencing of treatment has recently been examined, with two recent randomised trials examining the role of neoadjuvant therapy. As the article by Body *et al.* will discuss (12), the results, although still immature, are promising. There remain several limitations, not least of which is the inaccuracy of preoperative staging and the risk of overtreatment. Nevertheless, should an improvement in survival be demonstrated once these data mature, moving chemotherapy entirely into the neoadjuvant setting has the potential to improve survival without waiting for discovery of new drugs. Another potential benefit is the reduction of overall costs to health systems, as a consequence of decreasing rates of relapse and death.

Surgery

Surgery remains the core modality for cure of patients with colorectal cancers. There are several situations where standard surgical management is complicated by tumor characteristics. The classic of these is the locally invasive “T4” tumour, invading outside of the colorectum and into neighboring structures, as discussed in the excellent review by Dr. Gosavi and colleagues (13). The initial challenge lies in adequate preoperative staging to determine the appropriate management approach, followed by selection of appropriate neoadjuvant therapies and finally optimal surgical approach.

At the other end of the spectrum, there is the challenge of managing very early stage colorectal cancers detected by screening with the risk of both over- and under-treatment being difficult to balance for these otherwise well patients. Dr. Suhardja and colleagues demonstrate the uncertainties raised when managing these early stage patients and delineate the need for better evidence to guide treatment (14).

Stenting

A comprehensive overview of the role of colonic stenting in cancer patients is presented by Buxley and Chouhan (15), covering its role both as a means to palliate end stage large bowel obstruction but also as a ‘bridging treatment’ to more definite surgical intervention when appropriate. The paper reviews the current indications for stenting, optimal technique and the design principles of commercially available products. The timing of stenting, safety and pitfalls are discussed and the cases at the conclusion of the article serve to illustrate the complexities of decision making in this arena.

Conclusions

Colorectal cancer patients remain a large but underserved population with desperate need for significant improvements in outcomes, along with reduction in toxicity and lessening of impact in quality of life. Pending breakthroughs in new technology, optimization of existing infrastructure and techniques will best serve our patients.

We hope you find this special edition thought provoking and inspiring of further research in this field.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Digestive Medicine Research* for the series “Colorectal Cancer”. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://dx.doi.org/10.21037/dmr-21-42>). The series “Colorectal Cancer” was commissioned by the editorial office without any funding or sponsorship. ES served as the unpaid Guest Editor of the series and serves as an unpaid editorial board member of *Digestive Medicine Research* from Sep 2019 to Sep 2021. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Received: 14 April 2021; Accepted: 24 April 2021; Published: 30 June 2021.

doi: 10.21037/dmr-21-42

View this article at: <https://dx.doi.org/10.21037/dmr-21-42>

doi: 10.21037/dmr-21-42

Cite this article as: Body A, Chouhan H, Segelov E. Colorectal cancer—moving forward one step at a time. Dig Med Res 2021;4:23.