

Rectal cancer: a truly multidisciplinary challenge

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Over 40,000 people will be diagnosed with rectal cancer in the United States in 2014, and colorectal cancer remains the second leading cause of cancer death nationally despite renewed focus on diagnosis and management (1). That being said, the incidence of colorectal cancer has dropped significantly over the last several decades largely attributable to more successful screening programs (2). In addition, cancer-related mortality among those diagnosed with colorectal cancer has also dropped in recent years, which is likely a function of earlier intervention and improved treatment modalities (3).

The management of rectal cancer has evolved significantly over the last several decades and through this evolution, patients are now managed with a comprehensive multidisciplinary approach. From routine age-appropriate screening and history-taking through diagnostic work-up, cancer treatment, and survivorship, care of patients with rectal cancer requires a tremendous amount of resources and the expertise of an array of specialties working together to maximize patients' quality and quantity of life. In this focus issue, our contributors delve into the different aspects of rectal cancer prevention, treatment, and aftercare that are largely responsible for the reduced incidence and mortality associated with this disease.

After years of analysis, we now believe that as many as one in five patients diagnosed with colorectal cancer are genetically predisposed to developing invasive disease (4). Recognizing this at-risk population before they develop cancer, educating them, and enrolling them in proper screening protocols should help both in terms of disease prevention and earlier detection of invasive disease. In this issue, cancer genetics pioneer Dr. Lynch and fellow collaborators, Drs. Schluskel, Gagliano, Seto-Donlon, Eggerding, Donlon, and Berenberg have provided two

manuscripts which together provide a definitive look at the evolution of colorectal cancer genetics. Part 1 details the background and history of colorectal cancer genetics and how that information has been incorporated into clinical practice (5). In part 2, Dr. Schluskel *et al.* review the hereditary cancer syndromes and the clinical implications and impact that providers need to be aware of when formulating a management strategy for patients and their families (6).

For those patients that are diagnosed with rectal cancer, definitive treatment carries significant morbidity and mortality risks and techniques are continually being refined to reduce these treatment-related risks (7). As knowledge and understanding of rectal cancer continues to grow, identifying and screening at-risk populations in a timely fashion is leading to earlier detection and treatment. With earlier detection come more favorable outcomes and the potential to obviate the need for more traditional radical therapies. Drs. Heafner and Glasgow present a detailed review of the role of local excision in the treatment of early rectal cancers (8). In this review, the authors outline the rationale behind less invasive surgery in rectal cancer, the different techniques utilized, the risks and benefits associated with local excision, and the population that should be considered for this less invasive approach.

Despite improvements in screening, prevention, and early detection, a large portion of patients with rectal cancer present with more advanced stages of disease. For patients with locally advanced disease, treatment has long featured combined modality therapy given the propensity of rectal cancer to recur both locally and distantly. Internationally, numerous trials have sought to determine the optimal sequence, duration, and intensity of therapy in an attempt to maximize outcomes while limiting treatment-related

toxicities. In the United States, the standard of care in patients with locally advanced disease (at least T3 or node positive) is preoperative 5-fluorouracil-based chemotherapy concurrent with external beam irradiation to a dose of approximately 5,000 cGy followed by transabdominal resection 5-12 weeks after completion of neoadjuvant therapy followed by postoperative chemotherapy. This recommended course of therapy is based on the results of the German Rectal Cancer Study which showed improved local control rates and a more favorable morbidity profile with neoadjuvant chemoradiation when compared to adjuvant chemoradiation (9). Building on this and many other trials, there are several studies ongoing, and internationally, there continues to be much debate over the ideal sequencing of treatment. Dr. Fung-Kee-Fung explores the concept of combined modality therapy for locally advanced rectal cancer from a historical perspective, showing how we have arrived at the current standards and postulating on where we are heading in the future (10).

Local control following treatment is a major priority in rectal cancer both because of the historically high prevalence of local failure and due to the impact and morbidity associated with recurrent disease in the pelvis. Thus, many clinical trials for rectal cancer have focused on local control as a primary or secondary endpoint and based on the success of these studies, current treatment regimens yield long-term local control rates in excess of 90% (11). While local control rates in rectal cancer are now excellent, studies are finding that distant failure remains a persistent issue. There are a number of reasons to explain why, one being that after aggressive neoadjuvant chemoradiation and surgery, many patients never get their full course of adjuvant systemic therapy. In this issue, Drs. Boland and Fakih present the emerging role of neoadjuvant chemotherapy and how this change in therapy sequencing may further improve outcomes, particularly in terms of reducing rates of distant metastatic disease (12).

With improving systemic therapy approaches, refined surgical techniques, and emerging radiation technologies, patients with all stages of rectal cancer are experiencing better treatment outcomes than they had historically, even those with advanced stages of disease (3). Advances in systemic therapy have made long-term disease control a reality for patients with a small metastatic burden, opening the door for aggressive local therapy for the treatment of limited metastatic disease. The majority of studies investigating local treatment of metastatic colorectal cancer have focused on disease metastatic to the liver. The liver is

the most common site for colorectal metastases and spread to the liver is responsible for the majority of colorectal cancer-related deaths (13,14). In their manuscript, Drs. Clark and Smith lead a comprehensive discussion on liver-directed therapies in metastatic colorectal cancer (15). They take a step-wise approach to this complex treatment algorithm, focusing on the when, why and how of each treatment strategy along with the potential alternatives depending on the specific scenario.

Rectal cancer is a challenging disease, and as outlined above and throughout this issue, the treatments themselves can be quite complex. Over the course of treatment, there is a significant physical and emotional toll on patients and their loved ones. And with improving outcomes, more and more patients are becoming long term survivors of this disease. And while these improving outcomes are cause for excitement, there is often disease- and treatment-related morbidity which complicates their recovery and impacts on their post-treatment quality of life. From the perceived stigma of dealing with a permanent ostomy to chronic sexual dysfunction, patients face an array of life-altering morbidity in the post-treatment setting and these issues many times go undetected by providers and thus are left untreated. In this focus issue, Drs. Averyt and Nishimoto have developed two unique manuscripts designed to help providers understand what patients are going through after treatment and to provide them with tools to help break down the barriers that are often faced in colorectal cancer survivorship. The first manuscript focuses specifically on addressing the sexual dysfunction that patients face following diagnosis and treatment (16). This topic is often largely ignored by providers and patients are many times reluctant to address this subject on their own in their routine follow-up. The authors present very effective tools to aid clinicians in opening a dialogue with patients early on in their treatment course and throughout their therapy and the end result is getting these patients the help and therapy that they need and ultimately improving their quality of life. The second manuscript takes the reader into the mind of the patient, giving insight into the top 10 questions that patients may be thinking but not asking (17). This manuscript serves as a valuable reference for providers to utilize, helping them build a strong and trusting relationship with their patients.

As outlined, rectal cancer represents a comprehensive multidisciplinary challenge for many different providers who must work in concert to maximize the patient care experience. The goals of this focus issue of the *Journal of*

Gastrointestinal Oncology are to educate our readership about many of the issues that are faced when treating rectal cancer and to provide the necessary tools needed to enhance their care of these unique patients.

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