

Contents

Foreword: Colorectal Cancer	xiii
Timothy M. Pawlik	
Preface: Colorectal Cancer	xv
Traci L. Hedrick	
Colorectal Cancer: Preoperative Evaluation and Staging	127
Najjia N. Mahmoud	
<p>The preoperative assessment of patients with colorectal cancer (CRC) requires a multimodal approach, including endoscopic evaluation and clinical, radiographic, and biochemical assessment. In addition to providing a diagnosis, histologic review of biopsy specimens imparts valuable information about tumor grade and other important prognostic features that can help determine treatment. A thorough history and physical examination rounds out the initial evaluation and provides the surgeon and other treating physicians with vital additional information for detailed operative planning. Colon and rectal cancer, although closely related histologically, are considered, and often treated, very differently, depending on stage, based solely on location.</p>	
Early-Onset Colorectal Cancer	143
Valentine Nfonsam, Emily Wusterbarth, Amanda Gong, and Priyanka Vij	
<p>Colorectal cancer (CRC) is the third leading cause of cancer-related deaths in the United States, and the incidence of early-onset CRC (EOCRC, <50 years old) has been steadily increasing over the past 30 years. This article provides a comprehensive review of EOCRC traits, including incidence rates and patterns, tumor biologic differences compared to late-onset CRC, dietary risk factors, relationship between CRC and the microbiome, and patient survival outcomes associated with EOCRC. These factors carry importance in determining diagnostic, prognostic, disease monitoring, and treatment planning practices for EOCRC in the future. They also serve as guides for optimizing CRC screening recommendations.</p>	
Healthcare Disparities and Colorectal Cancer	157
Robert H. Hollis and Daniel I. Chu	
<p>Health care disparities are defined as health differences between groups that are avoidable, unnecessary, and unjust. Racial disparities in colorectal cancer mortality, particularly for Black patients, are well-described. Disparities in preventative measures, early detection, effective treatment, and posttreatment services contribute to these differences. Underlying these issues are patient, provider, health care system, and policy-level factors that lead to these disparities. Multilevel interventions designed to</p>	

address each level of care can provide an effective means to mitigate these disparities.

Nonoperative Management of Rectal Cancer: The Watch and Wait Strategy 171

Bruna Borba Vailati, Guilherme Pagin São Julião, Angelita Habr-Gama, and Rodrigo Oliva Perez

In recent decades, rectal cancer management has become increasingly challenging for multiple reasons. Proper imaging using dedicated magnetic resonance, standardization of total mesorectal excision, and incorporation of neoadjuvant treatment regimens have contributed to a significant decrease in local recurrence rates. The observation of complete tumor response to radiation or chemoradiation led to the proposal of organ-preservation strategies with avoidance of immediate surgery and close surveillance (Watch and Wait strategy) in selected patients. The purpose of this article is to review the current evidence related to the selection criteria and outcomes in patients enrolled in this Watch and Wait strategy.

Technological Advances in the Surgical Treatment of Colorectal Cancer 183

Sue J. Hahn and Patricia Sylla

Efforts toward standardization of surgical techniques have facilitated adoption of oncologic resections for colorectal cancer with associated improvement in outcomes. With the introduction of laparoscopy, total mesorectal excision (TME) and complete mesocolic excision (CME) techniques were progressively adapted to the minimally invasive surgery (MIS) approach with significant benefits with regards to patient recovery and comparable oncologic outcomes when performed by surgeons beyond their learning curve. Anastomotic complications and functional disturbances following TME remain significant. Recent innovations include intracorporeal anastomosis, which avoids midline extraction sites, and transanal TME, which lowers conversion rates and facilitates sphincter preservation for low rectal tumors.

Local Excision and Endoscopic Strategies for the Treatment of Colorectal Cancer 219

Ilker Ozgur and Emre Gorgun

Local excision and endoluminal surgery are organ preservation techniques, which are more widely accepted and practiced in colorectal cancer management. Although endoluminal surgery is considered challenging, it will continue to progress and gain more popularity over time. Increased education, research, and availability of the tools to perform these procedures will help more endoscopists be adept over time. Owing to the ability to avoid intraabdominal surgery, endoluminal surgery can be the next big step for minimally invasive surgery. Through research and development, fully flexible endorobotic platforms with stable camera positioning and precision will become a reality and push endoluminal surgery forward.

Surgical Principles of Rectal Cancer

239

Ebram Salama, Jessica Holland, and Marylise Boutros

This article reviews the oncological principles of rectal cancer surgery, beginning with an overview of the pertinent rectal and pelvic anatomy, followed by a discussion of the historical evolution in surgical management. Evidence supporting current practices with respect to proximal, distal, and circumferential margins are reviewed. Finally, operative approaches to restorative proctectomies and abdominoperineal resections are highlighted.

Targeted Therapy for Colorectal Cancer

255

Shinichiro Sakata and David W. Larson

Metastatic colorectal cancer (mCRC) is incurable in patients with unresectable disease. For most patients, the primary treatment is palliative systemic chemotherapy. Genomic profiling is used to detect specific genetic mutations that may offer selected patients a modest survival benefit with targeted therapy. Patients with mCRC with KRAS/NRAS/BRAF wild-type left-sided tumors may benefit from epidermal growth factor receptor (EGFR) inhibition with either cetuximab or panitumumab, in conjunction with chemotherapy. EGFR inhibitors can extend survival by 6 months compared with chemotherapy alone. The vascular endothelial growth factor (VEGF) inhibitor bevacizumab can serve as an alternative to EGFR inhibitors in right-sided tumors or second-line therapy. Many patients will have RAS mutations, and targeted therapies will not provide any benefit. The PRIME trial demonstrated that the addition of panitumumab to FOLFOX was associated with reduced overall survival. Patients with BRAF mutations do not benefit from targeted therapy unless a BRAF inhibitor supplements treatment. Triple combination therapy with cetuximab, the BRAF inhibitor encorafenib, and the MEK kinase inhibitor binimetinib has extended overall survival by about 3 months compared with chemotherapy alone. Finally, for the minority patients with microsatellite instability (MSI) high/mismatch repair (MMR) deficient tumors, either due to Lynch syndrome or sporadic mutations, immunotherapy is recommended as first-line treatment. The KEYNOTE-177 trial demonstrated that therapy with single-agent pembrolizumab improved progression-free survival by 8 months compared with FOLFOX or FOLFIRI and with or without EGFR inhibition. At this time, targeted therapy should only be used in patients with unresectable metastatic disease.

Management of Synchronous Colorectal Cancer Metastases

265

Traci L. Hedrick and Victor M. Zaydfudim

The management of patients with metastatic colorectal cancer (CRC) has evolved significantly over the last decade owing to advances in aggressive multimodality chemotherapy options, targeted therapy, development of sophisticated operative techniques, and adjunct radiotherapy options. Patients with synchronous CRC require complex decision-making with multidisciplinary collaboration to develop individualized treatment strategies taking into account tumor biology and patients' individual goals and objectives. We will outline important considerations with regard to treatment options for patients with synchronous metastatic CRC to facilitate

contemporary evidence-based management decisions and optimize oncologic outcomes.

Neoadjuvant Therapy for Rectal Cancer

279

Felipe F. Quezada-Diaz and J. Joshua Smith

The treatment of locally advanced rectal cancer is challenging and requires a multidisciplinary approach. Neoadjuvant treatment has improved local control by the combination of radiotherapy, surgery, and chemotherapy. However, neoadjuvant treatment has not yet been shown to improve overall survival and is associated with toxicities and late sequelae that impair the quality of life of patients. Currently, different types of neoadjuvant strategies have raised the question about which one is the optimal strategy for rectal cancer treatment. In this article, we explore the different neoadjuvant treatment regimens currently available, their associated benefits and toxicities, and novel approaches in this area.

Complete Mesocolic Excision and Extent of Lymphadenectomy for the Treatment of Colon Cancer

293

Tsuyoshi Konishi and Y. Nancy You

Curative-intent surgical resection of colon cancer involves optimal approaches to the peri-tumoral tissue, the mesocolon, and the draining lymph nodes. The key corresponding concepts that will be discussed are complete mesocolic excision (CME), central vascular ligation (CVL) or D3 dissection, and circumferential resection margin (CRM). We aim to describe these techniques and delineate evidence surrounding their technical feasibility, pathologic detail, as well as long-term oncologic impact. CME with CVL and D3 dissection are overlapping concepts both emphasizing anatomy-based resection of tumor and regional lymph nodes that does not breach the embryonic visceral fascia and ensures complete lymph node dissection up to the mesenteric root. Completeness of the mesocolic plane, number of harvested nodes, and CRM are surgical pathologic parameters that impact oncologic outcome. Attention to these details has been associated with improved outcomes in retrospective observational trials and the choice of open or minimally invasive approaches must be determined by surgeon's technical experiences.

Management of Colorectal Cancer in Hereditary Syndromes

307

Lisa A. Cunningham, Alessandra Gasior, and Matthew F. Kalady

Approximately 5% of all colorectal cancers develop within a hereditary colorectal cancer syndrome. Patients and families with these syndromes have an increased risk of colorectal and extracolonic cancers that develop at an early age. Recognition and diagnosis of these conditions are crucial to management and risk reduction. Surgeons must be aware of the unique aspects of the timing and extent of surgery (both therapeutic and prophylactic) within these syndromes, particularly for the most common syndromes, Lynch syndrome and familial adenomatous polyposis.