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Interdisciplinary Diagnosis and Management of Colorectal Cancer for Nursing, Radiology, Laboratory, Nutrition, and Health Informatics Professionals

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Abstract

Colorectal cancer (CRC) remains a significant global health burden, ranking as the third most commonly diagnosed malignancy and the second leading cause of cancer-related mortality worldwide. The complex molecular landscape, heterogeneous presentation, and multifaceted treatment approaches necessitate a collaborative, interdisciplinary framework for optimal patient outcomes. This comprehensive review synthesizes current evidence on CRC pathophysiology, risk factors, diagnostic modalities, and therapeutic strategies while emphasizing the critical roles of nursing, radiology, laboratory medicine, and health informatics professionals in the multidisciplinary care team. Recent advances in genomics, epigenetics, metabolic reprogramming, and artificial intelligence have revolutionized CRC diagnosis and management, creating both opportunities and challenges for healthcare professionals across specialties. The integration of molecular biomarkers, advanced imaging techniques, patient-derived organoids, and computational approaches has enabled more precise risk stratification, early detection, and personalized treatment selection. However, disparities in screening participation, healthcare access, and implementation of novel technologies persist. This review provides a framework for interdisciplinary collaboration, highlighting how nursing professionals can optimize patient education and supportive care, radiology experts can enhance diagnostic accuracy through advanced imaging and radiomics, laboratory specialists can facilitate molecular characterization and biomarker-guided therapy, and health informatics professionals can leverage artificial intelligence and data integration to improve clinical decision-making. By fostering effective communication and coordinated care across disciplines, healthcare systems can address the multifaceted challenges of CRC management and improve patient outcomes.

Keywords: Colorectal cancer, interdisciplinary care, nursing, radiology, laboratory medicine, health informatics, molecular diagnostics, artificial intelligence, targeted therapy, precision medicine.

Introduction

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Colorectal cancer represents one of the most common malignant neoplasms globally, with approximately 1.93 million new cases and 935,000 deaths reported in 2020, accounting for approximately 10% of all cancer diagnoses worldwide [1]. The disease burden is projected to increase by 63% by 2040, with particularly concerning trends in low-to-middle-income countries undergoing rapid urbanization and westernization of dietary patterns [2]. Countries with high Human Development Index values report the highest age-standardized incidence rates, exceeding 40 cases per 100,000 individuals in regions such as Europe, North America, and Australia [1]. However, the epidemiological landscape is shifting, with Japan exemplifying this transition—the age-standardized incidence rate has reached 45.5 per 100,000 for men and 28.5 per 100,000 for women, reflecting the adoption of Western dietary habits while maintaining higher incidence rates than the United States, suggesting the influence of additional genetic and environmental factors [3]. The pathophysiology of CRC is characterized by substantial heterogeneity, arising from the cumulative effects of genetic and epigenetic alterations that drive malignant transformation through at least three major molecular pathways: chromosomal instability (CIN),

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microsatellite instability (MSI), and the CpG island methylator phenotype (CIMP) [4]. The traditional adenoma-carcinoma sequence, involving sequential mutations in genes such as adenomatous polyposis coli (APC), Kirsten rat sarcoma viral oncogene homolog (KRAS), and tumor protein 53 (TP53), accounts for 70-90% of cases [5]. However, approximately 15% of CRCs develop through the serrated pathway, characterized by BRAF mutations and extensive DNA methylation [6]. This molecular diversity underpins the variable clinical presentations, treatment responses, and prognoses observed among CRC patients, necessitating personalized approaches to diagnosis and management.

Recent advances in molecular pathology have led to the identification of four consensus molecular subtypes (CMS): CMS1 (MSI immune), CMS2 (canonical), CMS3 (metabolic), and CMS4 (mesenchymal) [7]. This classification system provides a robust framework for understanding CRC biology and guiding clinical decision-making, as each subtype exhibits distinct molecular characteristics, immune microenvironments, treatment sensitivities, and prognostic implications. The integration of this molecular taxonomy into clinical practice represents a paradigm shift from traditional histopathological classification toward precision oncology, requiring collaboration among laboratory specialists, pathologists, and clinical oncologists [8]. The management of CRC has evolved dramatically over the past two decades, with the emergence of targeted therapies, immunotherapies, and multimodal treatment approaches. Immune checkpoint inhibitors have demonstrated remarkable efficacy in MSI-high/deficient mismatch repair (dMMR) CRC, establishing immunotherapy as the standard first-line treatment for this subset of patients [9]. Targeted agents against BRAF V600E mutations, KRAS G12C mutations, and various other molecular alterations have expanded therapeutic options, while anti-angiogenic agents and epidermal growth factor receptor inhibitors continue to play important roles in metastatic disease management [10]. Despite these advances, challenges persist, including primary and acquired drug resistance, tumor heterogeneity, and the limited efficacy of immunotherapy in the majority of CRC patients with microsatellite-stable tumors [11]. The complexity of contemporary CRC management demands a truly interdisciplinary approach, integrating the expertise of healthcare professionals across multiple specialties. Nursing professionals play a pivotal role in patient education, symptom management, and supportive care throughout the cancer trajectory. Radiology specialists contribute essential diagnostic and staging information through advanced imaging modalities and increasingly through radiomics and artificial intelligence applications. Laboratory medicine professionals facilitate molecular characterization, biomarker testing, and therapeutic drug monitoring. Health informatics specialists enable the integration and analysis of diverse data sources, supporting clinical decision-making and population health management. This review aims to synthesize current evidence on CRC diagnosis and management while providing a comprehensive framework for interdisciplinary collaboration that optimizes patient outcomes.

2. Etiology and Risk Factors

2.1 Genetic Predispositions and Hereditary Syndromes

Genetic factors play a crucial role in CRC development, with hereditary syndromes accounting for approximately 5% of all cases. Lynch syndrome, the most common hereditary CRC syndrome, results from germline mutations in mismatch repair genes (MLH1, MSH2, MSH6, PMS2) and confers a 50-80% lifetime risk of CRC [12]. These mutations lead to microsatellite instability and an increased risk of multiple cancers, including endometrial, ovarian, and gastric malignancies. Familial adenomatous polyposis, caused by APC gene mutations, is characterized by the development of hundreds to thousands of colorectal adenomas, with nearly 100% lifetime risk of CRC if untreated, typically manifesting before age 40 [12]. The expanding use of cancer gene panel testing in countries like Japan has facilitated earlier identification of these hereditary syndromes, enabling more intensive surveillance and personalized prevention strategies [3]. Beyond Mendelian syndromes, genome-wide association studies have identified numerous common genetic variants that modestly increase CRC risk. Single nucleotide polymorphisms in genes involved in inflammation, metabolism, and cell cycle regulation contribute to the polygenic component of CRC susceptibility [13]. The interplay between genetic predisposition and environmental factors, including diet, lifestyle, and gut microbiome composition, determines individual risk profiles. Understanding these genetic and environmental interactions is essential for developing personalized risk stratification approaches and targeted prevention strategies.

2.2 Dietary and Lifestyle Factors

Dietary patterns and lifestyle factors significantly influence CRC risk, with compelling evidence implicating processed meats, alcohol consumption, smoking, and obesity as modifiable risk factors. The International Agency for Research on Cancer has classified processed meats as Group 1 carcinogens, with meta-analyses demonstrating a 17% increased risk of CRC per 50 grams of daily consumption (relative risk [RR]=1.17, 95% CI:1.11-1.22) [14]. Red meat consumption also increases risk, particularly in Asian populations where meat intake has increased dramatically with westernization of diets. The Japan Public Health Center-based

Prospective Study found that high intake of red meat significantly increases colon cancer risk among Japanese women, while total meat consumption is associated with higher risk in Japanese men [15]. Alcohol consumption demonstrates a clear dose-response relationship with CRC risk, with heavy drinkers (>50 grams/day) facing a 44% increased risk (RR=1.44, 95% CI:1.25-1.65) compared to nondrinkers [16]. This association appears stronger in Japanese populations than in Western populations, possibly reflecting genetic polymorphisms in alcohol metabolism, particularly aldehyde dehydrogenase 2 variants [17]. Smoking is similarly associated with increased CRC risk and mortality, with current smokers having a 14-17% higher risk compared to never smokers, and the risk being dose-dependent on smoking duration and intensity [18]. The risk decreases after smoking cessation, emphasizing the importance of smoking prevention and cessation in CRC risk reduction strategies. Obesity significantly contributes to CRC risk, with every 5 kg/m² increase in body mass index associated with a 5% increased risk (RR=1.05, 95% CI:1.03-1.07) [19]. The mechanisms linking obesity to CRC include chronic low-grade inflammation, insulin resistance, altered adipokine profiles, and changes in gut microbiota composition. Interestingly, despite Japan having lower obesity rates than the United States, Japan's CRC incidence is higher, suggesting that additional factors, including genetic predisposition, differences in gut microbiota, and screening practices, may influence population-specific risk profiles [3].

2.3 Metabolic Conditions and Inflammatory Bowel Disease

Type 2 diabetes mellitus and insulin resistance are established risk factors for CRC, with meta-analyses demonstrating a 30% increased risk among diabetic individuals (RR=1.30, 95% CI:1.20-1.40) [20]. The hyperinsulinemia and insulin-like growth factor signaling associated with insulin resistance promote cell proliferation and inhibit apoptosis, contributing to colorectal carcinogenesis. In Japanese populations, higher plasma C-peptide levels have been significantly associated with increased CRC risk, particularly for colon cancer in men, with odds ratios of 2.3, 2.8, and 3.2 across ascending quartiles [21]. These findings underscore the importance of metabolic health in CRC prevention. Inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's disease, significantly elevates CRC risk through chronic inflammation-driven carcinogenesis. Meta-analyses of population-based cohort studies reveal a 2.4-fold increased risk of CRC in ulcerative colitis patients, with approximately 1.6% developing CRC during a 14-year follow-up [22]. Male IBD patients face higher risk than females, and those with extensive colitis have a 5.7-fold increased risk. Unlike sporadic CRC, IBD-associated cancer follows a distinct sequence from inflammation to dysplasia to carcinoma, characterized by early TP53 mutations and involvement of inflammatory pathways including nuclear factor kappa B and IL-6/STAT3 signaling [23]. IBD patients tend to develop CRC at a younger age, are more likely to have right-sided tumors, and experience higher rates of synchronous and metachronous tumors, necessitating specialized surveillance protocols [24].

3. Pathophysiology and Molecular Mechanisms

3.1 Genetic Alterations and Signaling Pathways

CRC development results from the sequential accumulation of genetic alterations that activate oncogenes and inactivate tumor suppressor genes, following the classic adenoma-carcinoma sequence proposed by Fearon and Vogelstein [25]. The initiation of colorectal tumorigenesis typically involves inactivation of the APC tumor suppressor gene, occurring in more than 80% of sporadic colorectal tumors [4]. APC mutations lead to aberrant activation of the Wnt/β-catenin signaling pathway, promoting cell proliferation and inhibiting apoptosis, representing a crucial early step in benign polyp formation [26]. Subsequent activation of KRAS mutations, occurring in approximately 40-50% of CRCs, drives sustained signaling through the RAS-RAF-MEK-ERK and PI3K-AKT-mTOR pathways, facilitating adenomatous polyp formation and expansion [27]. The progression from advanced adenomas to invasive carcinoma involves additional genetic alterations, including mutations in TP53, SMAD4, and other tumor suppressor genes. TP53, known as the "guardian of the genome," is the most commonly mutated gene in human cancers, with mutations occurring in approximately 50-60% of CRCs [4]. TP53 inactivation impairs DNA damage response, cell cycle arrest, and apoptosis, enabling cells with accumulating genetic abnormalities to survive and proliferate, promoting the development of aggressive cancers [28]. SMAD4 mutations and loss of heterozygosity on chromosome 18q affect transforming growth factor beta signaling, influencing cell migration, invasion, and epithelial-mesenchymal transition [25]. The chromosomal instability pathway, present in approximately 85% of sporadic CRCs, is characterized by abnormal chromosome number and structure, loss of heterozygosity at tumor suppressor loci, and somatic copy number alterations [4]. This pathway leads to genomic instability and tumor heterogeneity, contributing to therapy resistance and disease progression. In contrast, the MSI pathway, arising from DNA mismatch repair dysfunction, accounts for approximately 15% of sporadic CRCs and most Lynch syndrome-associated tumors [6]. MSI-high tumors exhibit hypermutation, producing numerous neoantigens that activate immune responses, explaining their exceptional responsiveness to immune checkpoint inhibitors [9].

3.2 Epigenetic Alterations

Epigenetic modifications, including DNA methylation, histone modifications, and non-coding RNA regulation, play increasingly recognized roles in

CRC pathogenesis. DNA methylation is the most well-studied epigenetic alteration in CRC, with genome-wide hypomethylation and CpG island promoter hypermethylation representing characteristic patterns [29]. Global hypomethylation, particularly affecting retrotransposons such as long interspersed nuclear element-1, leads to genomic instability and is associated with poor prognosis. Conversely, hypermethylation of CpG islands in promoter regions silences tumor suppressor genes and DNA repair genes, mimicking the effects of genetic mutations [30]. The CpG island methylator phenotype represents a distinct CRC subtype characterized by widespread promoter methylation, frequently co-occurring with BRAF mutations and MSI-high status. CIMP-high tumors exhibit hypermethylation of MLH1 and other key genes, leading to MMR deficiency and the development of tumors with unique clinical features [29]. Histone modifications, including acetylation and methylation, also contribute to CRC pathogenesis by regulating chromatin accessibility and gene expression. Dysregulation of histone acetyltransferases and deacetylases, as well as histone methyltransferases and demethylases, has been implicated in CRC progression [31]. Non-coding RNAs, including microRNAs and long non-coding RNAs, regulate gene expression through post-transcriptional mechanisms and epigenetic interactions. MicroRNA dysregulation frequently occurs in CRC, with certain microRNAs acting as oncogenes or tumor suppressors by targeting key genes in cancer-related pathways [30]. Long non-coding RNAs, such as HOTAIR and MALAT1, mediate epigenetic modifications through interactions with chromatin-modifying complexes, contributing to CRC proliferation, metastasis, and drug resistance [32]. Understanding these epigenetic mechanisms has opened new avenues for therapeutic targeting and biomarker development.

3.3 Metabolic Reprogramming

Metabolic reprogramming is a hallmark of cancer, enabling tumor cells to meet the energy and biosynthetic demands of rapid proliferation within dynamic microenvironments. The Warburg effect, characterized by elevated glycolysis even in the presence of oxygen, represents a defining feature of CRC glucose metabolism [33]. Glycolytic enzymes and transporters, including hexokinase, lactate dehydrogenase, and glucose transporter 1, are upregulated in CRC, correlating with poor prognosis [34]. Oncogenic signaling pathways, including Wnt/β-catenin, KRAS, and PI3K-AKT, regulate glucose metabolism, promoting the Warburg effect and supporting tumor growth [35]. Lipid metabolism is also reprogrammed in CRC, with increased fatty acid synthesis, uptake, and oxidation. Fatty acid synthase, a key enzyme in de novo lipogenesis, is highly expressed in primary CRC and liver metastases, and its expression correlates with poor prognosis [36]. ATP-citrate lyase, which converts citrate to acetyl-CoA, promotes CRC metastasis through interactions with β-catenin signaling [37]. Fatty acid oxidation, mediated by enzymes such as carnitine palmitoyltransferase 1A, supports energy production and redox homeostasis, protecting CRC cells from oxidative stress and facilitating metastasis [38]. Amino acid metabolism, particularly glutamine metabolism, is significantly altered in CRC. Glutamine addiction, characterized by increased glutamine uptake and utilization, provides nitrogen and carbon for nucleotide and protein synthesis, as well as supporting the tricarboxylic acid cycle [39]. KRAS-mutant CRC exhibits reprogrammed glutamine metabolism through transporter expression modulation and activation of Wnt signaling, promoting malignant progression [40]. Understanding metabolic vulnerabilities in CRC has led to the development of metabolic inhibitors as therapeutic strategies, including glutaminase inhibitors and fatty acid synthase inhibitors, which are currently being evaluated in clinical trials [41].

4. Diagnostic Approaches and Interdisciplinary Collaboration

4.1 Role of Laboratory Medicine in Molecular Diagnostics

Laboratory medicine professionals play a central role in CRC diagnosis, molecular characterization, and treatment selection. The diagnostic workup begins with histopathological examination of biopsy specimens obtained during colonoscopy, which confirms the diagnosis, determines histologic subtype, and provides information on tumor grade and differentiation. However, contemporary CRC diagnosis extends far beyond conventional histopathology, incorporating extensive molecular testing to guide treatment decisions [42]. Microsatellite instability testing and mismatch repair protein immunohistochemistry are essential for identifying patients eligible for immunotherapy. The landmark KEYNOTE-177 trial established pembrolizumab as standard first-line treatment for MSI-high/dMMR metastatic CRC, demonstrating significantly improved progression-free survival compared to chemotherapy (16.5 vs. 8.2 months) [9]. Laboratory professionals must ensure accurate MSI/dMMR testing using validated methodologies, including polymerase chain reaction-based MSI analysis and immunohistochemical staining for MLH1, MSH2, MSH6, and PMS2 proteins. Reflex testing for BRAF V600E mutations and MLH1 promoter methylation may be performed to distinguish sporadic MSI-high tumors from Lynch syndrome-associated tumors [6]. RAS mutation testing is essential for guiding anti-EGFR therapy, as KRAS and NRAS exon 2, 3, and 4 mutations predict resistance to cetuximab and panitumumab.

Approximately 40-50% of CRCs harbor KRAS mutations, and testing is recommended for all patients with metastatic disease [27]. BRAF V600E mutations, present in approximately 8-10% of CRCs, identify a subgroup with poor prognosis and guide use of BRAF inhibitor combinations, including encorafenib and cetuximab [10]. HER2 amplification and NTRK gene fusions, though less common, represent actionable targets in CRC, with trastuzumab-based therapies and NTRK inhibitors available for select patients [43]. Laboratory specialists must also ensure accurate assessment of tumor mutational burden, which may identify patients likely to benefit from immunotherapy even in the absence of MSI-high status. Comprehensive genomic profiling using next-generation sequencing enables simultaneous detection of multiple actionable alterations, facilitating personalized treatment selection [44]. However, challenges remain, including the need for standardized testing protocols, quality assurance programs, and efficient communication of results to the clinical care team.

4.2 Role of Radiology in Diagnosis, Staging, and Response Assessment

Radiology professionals contribute essential information for CRC diagnosis, staging, treatment planning, and response assessment. While colonoscopy with biopsy remains the gold standard for diagnosis, computed tomography (CT) colonography (virtual colonoscopy) offers a less invasive alternative for screening and diagnosis, particularly in patients unable to undergo conventional colonoscopy. CT and magnetic resonance imaging (MRI) provide crucial staging information, assessing tumor invasion depth (T stage), lymph node involvement (N stage), and distant metastases (M stage) [45]. For rectal cancer, MRI is the preferred imaging modality, providing high-resolution assessment of tumor extent, mesorectal fascia involvement, and extramural vascular invasion. This information is critical for selecting patients for neoadjuvant chemoradiotherapy and planning surgical resection. MRI-based risk stratification, including assessment of tumor regression after neoadjuvant therapy, helps guide treatment decisions and predict outcomes. Pelvic MRI also identifies enlarged lymph nodes and evaluates the circumferential resection margin, which is a key predictor of local recurrence [45]. CT imaging remains the primary modality for detecting distant metastases, particularly in the liver and lungs. Dual-energy CT and contrast-enhanced CT improve lesion detection and characterization, while CT perfusion imaging may provide functional information about tumor angiogenesis. PET/CT with 18F-fluorodeoxyglucose is valuable for detecting occult metastases, assessing treatment response, and evaluating suspected recurrence. However, PET/CT has limitations, including false-positive findings due to inflammation and variability in tracer uptake [46]. Recent advances in radiomics and artificial intelligence (AI) have enhanced the diagnostic and prognostic capabilities of medical imaging in CRC. AI algorithms, particularly deep learning models, can extract quantitative features from imaging data that reflect tumor heterogeneity, vascularity, and metabolic activity. These radiomic features have shown promise in predicting molecular subtypes, treatment response, and clinical outcomes, potentially enabling non-invasive characterization of tumor biology [47]. For example, radiomics-based biomarkers have been developed to predict tumor-infiltrating CD8+ cell status and response to PD-1/PD-L1 therapy based on CT features [48]. Radiology professionals must be familiar with these emerging technologies and collaborate with health informatics specialists to integrate AI tools into clinical practice.

4.3 Role of Nursing in Patient Care and Support

Nursing professionals are integral to the CRC care continuum, providing patient education, symptom management, and supportive care throughout diagnosis, treatment, and survivorship. The nursing role begins at diagnosis, where nurses provide education about the disease process, diagnostic procedures, and treatment options, addressing patient concerns and ensuring informed decision-making. Effective communication is essential, as CRC diagnosis often causes significant psychological distress, and nurses must provide emotional support and connect patients with appropriate resources [49]. During treatment, nurses manage the complex symptom burden associated with CRC therapies, including chemotherapy-related adverse effects such as nausea, vomiting, fatigue, neuropathy, and diarrhea. They implement evidence-based interventions to prevent and manage these symptoms, administer chemotherapy and supportive medications, and monitor for complications. Nursing assessments are crucial for early detection of treatment-related toxicities, including febrile neutropenia, electrolyte imbalances, and organ dysfunction, enabling timely interventions to prevent serious adverse events [50]. Nurses also play a critical role in managing the unique supportive care needs of CRC patients, including ostomy care, nutritional support, and psychological counseling. For patients undergoing surgical resection, nurses provide preoperative education, postoperative monitoring, and ostomy care training, helping patients adapt to physical changes and maintain quality of life. Nutritional counseling is essential for patients experiencing weight loss, malabsorption, or side effects affecting dietary intake, with nurses collaborating with dietitians to develop personalized nutritional plans [50]. In the era of precision medicine, oncology nurses must understand the implications of molecular testing, targeted therapies, and immunotherapies to provide effective patient education and management. They must recognize the unique toxicity profiles of targeted agents and immunotherapies, including immune-related adverse events that require prompt recognition and management. Nurses also coordinate care across the

interdisciplinary team, ensuring effective communication and continuity of care, and address the psychosocial and supportive care needs of patients and families throughout the cancer trajectory [49].

5. Treatment Modalities and Therapeutic Advances

5.1 Surgical and Locoregional Therapies

Surgical resection remains the cornerstone of curative treatment for localized CRC, with the goal of complete tumor removal with negative margins. For colon cancer, segmental colectomy with adequate lymphadenectomy is standard, with the extent of resection determined by tumor location and blood supply. Laparoscopic and robotic approaches have gained acceptance, offering reduced postoperative pain, shorter hospital stays, and comparable oncologic outcomes to open surgery [51]. For rectal cancer, total mesorectal excision is the surgical standard, providing optimal local control and preservation of pelvic autonomic function. Neoadjuvant chemoradiotherapy is standard for locally advanced rectal cancer (T3/T4 or node-positive), improving local control and downstaging tumors to facilitate sphincter preservation. This approach is associated with increased rates of pathologic complete response, particularly in MSI-high tumors, which are more radio-sensitive [52]. Neoadjuvant chemotherapy is increasingly utilized for colon cancer with high-risk features, such as T4 tumors, with the aim of achieving downstaging, improving surgical margins, and reducing the risk of distant recurrence. Ongoing clinical trials are evaluating total neoadjuvant therapy—combining chemotherapy and chemoradiotherapy—for rectal cancer, which has shown promising results in increasing pathologic complete response rates [51]. For patients with liver-limited or lung-limited metastases, surgical resection and local ablative therapies—including radiofrequency ablation, microwave ablation, and stereotactic body radiotherapy—can achieve prolonged survival and potential cure. Multidisciplinary tumor boards, involving surgeons, medical oncologists, radiation oncologists, radiologists, and pathologists, are essential for selecting patients who may benefit from these aggressive local therapies. The integration of systemic therapies, including chemotherapy and targeted agents, with local therapies has improved outcomes for patients with oligometastatic disease [51].

5.2 Systemic Therapies

Systemic chemotherapy remains the backbone of treatment for metastatic CRC and high-risk stage III disease. The cytotoxic agents 5-fluorouracil, leucovorin, oxaliplatin, and irinotecan form the foundation of combination regimens, including FOLFOX, FOLFIRI, and FOLFOXIRI. The choice of regimen depends on patient factors, tumor characteristics, and treatment goals. The addition of bevacizumab, a VEGF inhibitor, to chemotherapy has demonstrated survival benefits in metastatic CRC, and anti-EGFR agents, including cetuximab and panitumumab, are effective in RAS wild-type tumors [53]. Targeted therapies have expanded treatment options for CRC patients with specific molecular alterations. BRAF V600E inhibitors, including encorafenib, have shown efficacy when combined with cetuximab, with or without MEK inhibition, in patients with BRAF-mutant CRC. The BEACON CRC trial demonstrated significantly improved overall survival and response rates with encorafenib-cetuximab combinations compared to standard therapy [10]. KRAS G12C inhibitors, recently approved for non-small cell lung cancer, are being evaluated in CRC, with promising activity in combination with EGFR inhibitors. Other emerging targets include HER2 amplification, NTRK fusions, and RET fusions, with approved agents available for these molecular subsets [43]. Immunotherapy has revolutionized the treatment of MSI-high/dMMR CRC, with checkpoint inhibitors targeting PD-1/PD-L1 and CTLA-4 achieving durable responses in metastatic disease. Pembrolizumab, nivolumab, and combination nivolumab-ipilimumab are approved for MSI-high CRC, with objective response rates of 30-55% in previously treated patients and even higher rates in the first-line setting. The KEYNOTE-177 trial established pembrolizumab as standard first-line therapy for MSI-high metastatic CRC, with a progression-free survival of 16.5 months compared to 8.2 months for chemotherapy [9]. However, only 5% of CRC patients have MSI-high tumors, and immunotherapy has limited efficacy in MSS CRC, highlighting the need for strategies to overcome resistance [11].

5.3 Emerging Therapeutic Approaches

Several emerging therapeutic approaches hold promise for improving CRC outcomes. Metabolic inhibitors targeting glutamine metabolism, fatty acid synthesis, and glycolysis are being evaluated in preclinical and early clinical studies. The glutaminase inhibitor CB-839 has shown antitumor activity in PIK3CA-mutant CRC, particularly in combination with 5-fluorouracil, and is being evaluated in clinical trials [41]. Fatty acid synthase inhibitors, including TVB-2640, have demonstrated preclinical activity in CRC and are being investigated in combination with standard chemotherapies. Epigenetic therapies targeting DNA methylation and histone modifications represent another promising approach. DNA methyltransferase inhibitors, including azacitidine and decitabine, have shown activity in preclinical studies and early clinical trials, particularly in combination with chemotherapy or immunotherapy. Histone deacetylase inhibitors, such as vorinostat and panobinostat, have demonstrated antitumor effects in CRC cell lines and may overcome drug resistance through epigenetic modulation [31]. The reversible

nature of epigenetic changes makes these targets particularly attractive, and ongoing research is exploring optimal combinations and patient selection strategies. Patient-derived tumor organoids have emerged as powerful platforms for drug development and personalized treatment selection. Organoids accurately replicate the genetic and phenotypic characteristics of primary tumors, enabling drug sensitivity testing and identification of effective therapies for individual patients [54]. The development of organoid biobanks has facilitated large-scale screening of drug candidates and investigation of drug resistance mechanisms. Organoid-based drug sensitivity assays have shown correlation with clinical responses, suggesting their potential utility for guiding treatment decisions [55]. However, challenges remain, including standardization of culture methods, long-term stability, and clinical implementation.

6. Role of Artificial Intelligence and Health Informatics

6.1 AI in CRC Diagnostics and Biomarker Prediction

Artificial intelligence, particularly machine learning and deep learning, has transformative potential in CRC diagnosis and management. AI algorithms can analyze diverse data types, including genomic, pathological imaging, and clinical information, to discover new biomarkers and therapeutic targets. In pathology, AI can autonomously identify tumor cells and microenvironment features in histopathological slides, aiding pathologists in diagnosis and classification. Deep learning models can predict MSI/dMMR status directly from hematoxylin-eosin-stained slides, with high accuracy, potentially reducing the need for expensive and time-consuming molecular testing [56]. AI-based image analysis has been applied to predict CMS subtypes from routine histopathology slides, enabling molecular classification without RNA sequencing. Sirinukunwattana et al. developed an image-based consensus molecular subtype classifier that demonstrated high accuracy and generalization across multiple cohorts [57]. Similarly, deep learning models have been developed to predict key mutations, including BRAF, KRAS, and TP53, from histopathology images, with potential applications in resource-limited settings where molecular testing may not be available. Social network analysis of cell networks has enhanced prediction of molecular pathways and key mutations in CRC, demonstrating the value of integrating cellular spatial information into deep learning models [58]. In radiology, AI algorithms can analyze CT, MRI, and PET images, improving diagnostic accuracy and efficiency. Radiomics-based biomarkers, extracted through machine learning, have shown promise in predicting tumor characteristics, treatment response, and prognosis. For example, AI-driven pathological image analysis can assess the tumor immune microenvironment, identifying patterns associated with immunotherapy response and providing more accurate and reproducible evaluations than conventional immunohistochemistry [59]. However, challenges remain, including data quality issues, algorithm interpretability, and the need for rigorous clinical validation.

6.2 AI in Treatment Selection and Response Prediction

AI algorithms hold considerable promise in predicting treatment responses, integrating clinical, genomic, transcriptomic, and imaging data to forecast patient outcomes and guide treatment decisions. Machine learning models can predict responses to immunotherapy by analyzing tumor mutational burden, MSI status, PD-L1 expression, and immune microenvironment characteristics. Radiomics-based biomarkers have been developed to predict tumor-infiltrating CD8+ cell status and response to PD-1/PD-L1 therapies based on CT features [48]. Such tools facilitate patient stratification and enable more personalized treatment selection. In targeted therapy, AI can identify patients likely to benefit from specific agents based on molecular profiles and predict mechanisms of resistance. For example, AI analysis of genomic data can identify co-occurring mutations that may confer resistance to EGFR inhibitors, helping clinicians select appropriate therapeutic strategies. AI can also predict chemotherapy efficacy and side effects based on genetic and clinical information, optimizing treatment plans and minimizing toxicity [60]. The integration of AI with multi-omics data enables comprehensive analysis of tumor biology and treatment responses, paving the way for precision medicine. Machine learning approaches have been applied to predict clinical outcomes in CRC, including recurrence risk and overall survival. Multi-stain deep learning models, trained on large cohorts, have demonstrated superior prognostic accuracy compared to conventional approaches, aiding in treatment planning and patient counseling [61]. These models can be integrated into clinical workflows, providing decision support to clinicians and facilitating personalized care. However, the clinical translation of AI models faces challenges, including the need for rigorous validation, regulatory approval, and integration with electronic health records.

6.3 Data Integration and Clinical Decision Support

Health informatics professionals play a crucial role in enabling the integration of diverse data sources—including genomic, imaging, clinical, and administrative data—to support clinical decision-making and population health management. The development of robust data infrastructure, including electronic health records, registries, and biobanks, is essential for facilitating research and quality improvement in CRC care. Health informatics specialists must ensure data quality, interoperability, and privacy, enabling effective use of data for clinical and research purposes [62]. Clinical decision support

systems, incorporating AI algorithms and evidence-based guidelines, can assist clinicians in diagnosis, treatment selection, and monitoring. These systems can integrate patient-specific data, including molecular test results and clinical characteristics, to generate personalized recommendations, improving adherence to guidelines and reducing variability in care. For example, AI-based systems can flag patients who may benefit from genetic counseling or immunotherapy based on molecular test results, or identify patients at high risk for adverse events who require more intensive monitoring [62]. Population health management approaches, facilitated by health informatics, are essential for addressing disparities in CRC screening, diagnosis, and treatment. Data analytics can identify communities with low screening rates, enabling targeted interventions and resource allocation. Integration of screening data with national cancer registries enables comprehensive surveillance and evaluation of screening program effectiveness. In Japan, population-based CRC screening programs have significantly improved early detection and reduced mortality, but challenges remain, including suboptimal participation rates and regional disparities in program implementation [3]. Health informatics professionals can support efforts to address these challenges through development of electronic reminder systems, patient portals, and data-driven quality improvement initiatives.

7. Interdisciplinary Collaboration and Care Coordination

7.1 Multidisciplinary Tumor Boards

Multidisciplinary tumor boards represent the cornerstone of interdisciplinary CRC care, bringing together medical oncologists, surgical oncologists, radiation oncologists, radiologists, pathologists, nurses, and other specialists to develop comprehensive, individualized treatment plans. These teams review complex cases, integrate diverse perspectives, and ensure that treatment recommendations incorporate all relevant clinical, pathological, and molecular information. The multidisciplinary approach has been associated with improved adherence to clinical guidelines, increased use of appropriate therapies, and better patient outcomes [63]. Effective tumor board functioning requires clear communication, defined roles, and standardized processes. Radiology professionals present imaging findings, including tumor extent, nodal status, and metastatic burden, while laboratory and pathology specialists present histopathological and molecular data, including MSI/dMMR status, RAS and BRAF mutation testing, and other relevant biomarkers. Medical oncologists discuss treatment options, including chemotherapy, targeted therapy, and immunotherapy, while surgical and radiation oncologists address locoregional treatment strategies. Nursing professionals provide valuable perspectives on patient preferences, functional status, and supportive care needs [63]. The integration of emerging technologies, including AI and decision support tools, can enhance tumor board functioning by providing additional insights and facilitating data synthesis. For example, AI-based imaging analysis can provide quantitative assessments of tumor characteristics, while decision support algorithms can identify relevant clinical trials or treatment options based on molecular profiles. Health informatics professionals can support these efforts by developing and maintaining data integration platforms and decision support tools, ensuring that relevant information is accessible and actionable [62].

7.2 Communication and Care Coordination Across Disciplines

Effective communication and care coordination across disciplines are essential for optimizing CRC outcomes, particularly given the complexity of contemporary treatment approaches and the multiplicity of healthcare professionals involved in patient care. Clear communication channels, including shared electronic health records, standardized reporting, and regular team meetings, facilitate information exchange and reduce the risk of errors or omissions. Standardized pathology and radiology reports, incorporating key information elements, ensure that critical data is effectively communicated to clinical colleagues [64]. Care coordination is particularly important during transitions between treatment phases, such as from neoadjuvant to surgical therapy, or from hospital to home. Nursing professionals often serve as care coordinators, ensuring that patients understand their treatment plans, have access to supportive services, and receive appropriate follow-up care. They facilitate communication between specialists, manage patient appointments and testing, and provide continuity of care throughout the cancer trajectory. Care coordination also involves connecting patients with supportive services, including nutrition counseling, psychological support, and palliative care, addressing the comprehensive needs of patients and families [50]. The use of patient navigation programs has been shown to improve CRC screening rates, reduce time to diagnosis and treatment, and enhance patient satisfaction. Patient navigators, often nursing professionals or trained laypersons, guide patients through the healthcare system, addressing barriers to care including transportation, language, and financial concerns. They also facilitate communication between patients and healthcare providers, ensuring that patients understand their diagnosis, treatment options, and care plans. Patient navigation is particularly important for underserved populations, who may face additional barriers to accessing care [64].

7.3 Shared Decision-Making and Patient Engagement

Shared decision-making, in which patients and healthcare professionals collaborate to make treatment decisions, is essential for ensuring that care aligns with patient values, preferences, and goals. Given the complexity of CRC treatment options and the potential for significant adverse effects, shared decision-making is particularly important. Healthcare professionals must communicate effectively with patients, providing clear, balanced information about treatment risks and benefits, and supporting informed decision-making. The integration of decision aids, including patient education materials and decision support tools, can facilitate shared decision-making [65]. Patient engagement is critical throughout the cancer trajectory, from prevention and screening to treatment and survivorship. Educating patients about CRC risk factors, screening options, and early warning signs is essential for promoting early detection and reducing mortality. Patient education materials, including written materials, videos, and web-based resources, should be available in multiple languages and health literacy levels, ensuring accessibility for diverse populations. Mobile health applications and patient portals can support patient engagement, enabling patients to access their health information, communicate with healthcare providers, and manage their care [65]. Nursing professionals play a central role in patient education and engagement, providing information and support at each stage of the cancer trajectory. They assess patient understanding, address concerns, and ensure that patients have the knowledge and resources necessary to make informed decisions. Nurses also provide ongoing support during treatment, addressing side effects, monitoring for complications, and helping patients navigate the healthcare system. The therapeutic relationship between nurses and patients is fundamental to effective cancer care, providing emotional support and fostering trust [49].

8. Challenges and Future Directions

8.1 Addressing Disparities in CRC Care

Despite advances in CRC diagnosis and treatment, significant disparities persist, influenced by socioeconomic status, geographic location, race, and ethnicity. Lower-income and less educated individuals often face limited access to preventive healthcare, leading to delayed diagnosis and treatment, and worse outcomes [1]. Regional disparities are evident even in Japan, where incidence and mortality rates vary significantly across prefectures, influenced by dietary habits, alcohol consumption, and lifestyle factors [3]. Addressing these disparities requires targeted public health initiatives, improved healthcare access, and community-based interventions tailored to specific populations. Screening participation remains suboptimal in many regions, with barriers including lack of awareness, limited access to healthcare, financial constraints, and fear of invasive procedures. In Japan, challenges include suboptimal participation rates in fecal immunochemical test screening and limited follow-up for individuals with positive results [3]. Effective strategies to improve screening uptake include community outreach, patient navigation, mobile screening programs, and financial incentives. Educational campaigns, particularly those tailored to cultural needs and supported by community health workers, have proven successful in improving screening uptake among underserved populations [64]. Integration of innovative technologies, such as smartphone-based reminders, can also enhance participation. Access to innovative therapies and molecular testing remains limited in many settings, particularly in low-to-middle-income countries. While MSI testing is recommended for all CRC patients to guide immunotherapy, access to testing is variable across regions. Similarly, comprehensive genomic profiling, required for identification of actionable alterations, is often limited by cost and infrastructure constraints. International collaboration and technology transfer are needed to address these disparities, ensuring that all patients benefit from advances in precision oncology [44].

8.2 Overcoming Treatment Resistance

Primary and acquired drug resistance represent major challenges in CRC treatment, limiting the efficacy of systemic therapies and contributing to disease progression. Mechanisms of resistance include intrinsic tumor heterogeneity, tumor microenvironment interactions, and adaptive responses to therapy. In immunotherapy, resistance mechanisms in MSS CRC include low tumor mutational burden, lack of tumor-infiltrating lymphocytes, and immunosuppressive tumor microenvironment [11]. Overcoming resistance requires combination strategies, including immunotherapy with targeted therapy, chemotherapy, or epigenetic modulators, which are being investigated in clinical trials. Targeted therapy resistance often arises through secondary mutations, bypass signaling pathways, or epithelial-mesenchymal transition. For example, BRAF inhibitor resistance in CRC occurs through feedback activation of EGFR, explaining the limited activity of BRAF inhibitors as monotherapy and the rationale for combination with EGFR inhibitors [10]. KRAS inhibitor resistance mechanisms include secondary KRAS mutations, upstream activation, and bypass signaling, requiring combination approaches or the development of next-generation inhibitors [43]. Understanding resistance mechanisms through genomic, transcriptomic, and functional studies is essential for developing strategies to overcome resistance. Patient-derived tumor organoids, which replicate the genetic and phenotypic characteristics of primary tumors, can model the evolution of drug resistance through long-term culture and exposure to increasing drug concentrations. Single-cell sequencing and proteomic analyses of drug-resistant organoids can identify resistant subpopulations and highlight key genes and pathways associated with resistance [54]. The organoid platform can also be used to screen drug combinations to

overcome resistance, providing evidence for clinical trial design and personalized treatment strategies [55]. Health informatics and AI approaches can integrate multi-omics data to predict resistance mechanisms and identify effective combination strategies.

8.3 Integration of Emerging Technologies into Clinical Practice

The integration of emerging technologies, including AI, organoids, and advanced molecular diagnostics, into clinical practice presents both opportunities and challenges. AI algorithms require validation on diverse, real-world datasets to ensure generalizability and avoid biases. Regulatory approval, clinical implementation, and integration with electronic health records pose logistical and financial challenges. Healthcare professionals must be trained to interpret AI outputs and incorporate them into clinical decision-making, requiring educational initiatives and practice changes. Ensuring data privacy and addressing ethical concerns, including algorithmic bias and accountability, are essential for responsible AI implementation [62]. Organoid technology faces challenges including standardization, long-term stability, and clinical implementation. Culture conditions for organoids are complex, requiring stringent quality control to ensure consistency. Long-term culture poses risks of genetic drift and phenotypic alterations, potentially affecting drug sensitivity predictions. Standardized protocols for organoid establishment, characterization, and drug sensitivity testing are needed to facilitate clinical use. Regulatory frameworks for organoid-based diagnostic testing are being developed, but remain limited [54]. Despite these challenges, organoid technology holds significant potential for personalized treatment selection, drug development, and mechanistic studies. The integration of multi-omics data, including genomics, transcriptomics, proteomics, and metabolomics, with clinical and imaging data, enables comprehensive characterization of CRC biology and treatment responses. Health informatics infrastructure is essential for managing large-scale data, integrating diverse sources, and enabling analysis through AI approaches. Data sharing and collaboration across institutions and countries are essential for accelerating research and clinical translation. International initiatives, such as the Cancer Moonshot in the United States, are driving advancements in early detection and precision medicine through collaborative research [62]. However, challenges remain, including data standardization, privacy concerns, and the need for robust validation of integrated approaches.

9. Conclusion

Colorectal cancer remains a significant global health challenge, with rising incidence in many regions and substantial mortality despite advances in diagnosis and treatment. The complex molecular heterogeneity of CRC, with distinct genetic, epigenetic, and metabolic alterations, necessitates personalized approaches that integrate diverse diagnostic modalities and therapeutic strategies. The evolution of CRC management from conventional histopathology to molecular taxonomy and precision oncology represents a paradigm shift, requiring interdisciplinary collaboration across multiple specialties. Nursing professionals are essential to the CRC care continuum, providing patient education, symptom management, and supportive care throughout diagnosis, treatment, and survivorship. They coordinate care across disciplines, ensuring effective communication and continuity, and address the comprehensive needs of patients and families. Radiology professionals contribute essential diagnostic and staging information through advanced imaging modalities and increasingly through radiomics and AI applications, enabling non-invasive characterization of tumor biology and treatment response. Laboratory medicine professionals facilitate molecular characterization, biomarker testing, and therapeutic drug monitoring, ensuring that treatment decisions are informed by accurate, timely molecular data. Health informatics professionals enable the integration and analysis of diverse data sources, supporting clinical decision-making through AI and data analytics, and addressing disparities in CRC care through population health management approaches. The integration of emerging technologies, including AI, organoids, and advanced molecular diagnostics, holds promise for improving CRC outcomes through more accurate diagnosis, personalized treatment selection, and identification of novel therapeutic targets. However, challenges remain, including disparities in access to care, drug resistance, and the need for rigorous validation and implementation of novel technologies. Addressing these challenges requires continued interdisciplinary research, collaboration, and commitment to patient-centered care. Future research should focus on understanding the interplay between genetic, epigenetic, and metabolic alterations, developing strategies to overcome drug resistance, and optimizing the integration of novel technologies into clinical practice. By fostering effective interdisciplinary collaboration and leveraging emerging technologies, healthcare systems can address the multifaceted challenges of CRC management and improve outcomes for patients worldwide.

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