

Diagnosis and Management of Colorectal Cancer in the Gulf Area: Current Practice and Future Suggestions from Expert Opinions

Humaid O Al-Shamsi¹⁻⁵, Kakil Rasul Snr⁶, Alaaeldin Shablak⁷, Abdulsalam AlNajjar⁸, Amrou Mamdouh abdeen Shabaan^{9,10}, Maha Al Sindi¹¹, Michael Nasr¹², Ali AlJabban¹², Saeed Rafii¹³

¹Department of Oncology, Burjeel Medical City, Abu Dhabi, United Arab Emirates; ²Department of Medical Oncology, College of Medicine, Ras Al Khaimah Medical and Health Sciences University, Ras Al Khaimah, United Arab Emirates; ³President of Emirates Oncology Society, Dubai, United Arab Emirates; ⁴Department of Medical Oncology, Gulf Medical University, Ajman, United Arab Emirates; ⁵Lead of Gulf Cancer Society, Alsaifa, Kuwait; ⁶Gastrointestinal and Hepatopancreatobiliary Unit, Hamad Medical Corporation, National Center for Cancer Care and Research (NCCCR), Doha, Qatar; ⁷Department of Medical Oncology, Hamad Medical Corporation, National Center for Cancer Care and Research (NCCCR), Doha, Qatar; ⁸Colorectal Cancer Unit, Kuwait Cancer Control Center, Kuwait City, Kuwait; ⁹Department of Medical Oncology, Kuwait Cancer Control Center, Kuwait City, Kuwait; ¹⁰Department of Clinical Oncology, Minia University, Minya, Egypt; ¹¹Department of Oncology, Salmaniya Medical Complex, Manama, Bahrain; ¹²Medical department, Pfizer Inc., Dubai, United Arab Emirates; ¹³Medical Oncology, Mediclinic City Hospital, Dubai, United Arab Emirates and Head of Research department at Emirates Oncology Society, Dubai, United Arab Emirates

Correspondence: Saeed Rafii, Medical Oncology, Mediclinic City Hospital, Dubai, United Arab Emirates and Head of Research department at Emirates Oncology Society, Dubai, United Arab Emirates, Email saeed.rafi@mediclinic.ae

Abstract: Colorectal cancer (CRC) is one of the most diagnosed cancers, leading to considerable cancer-related deaths globally. Recently, a notable increase has been observed in annual CRC incidence rates, particularly among individuals aged ≤ 50 years. Rapid urbanization and lifestyle changes have contributed to this trend. Early diagnosis through structured screening programs remains crucial for improving prognosis, yet uptake in the Gulf remains suboptimal due to limited public awareness and gaps in the national screening infrastructure. Diagnostic approaches in the region increasingly incorporate advanced imaging modalities and molecular testing, although access to in-house testing facilities is limited, often resulting in delays in personalized therapy initiation. Treatment strategies for CRC in the Gulf are guided by international guidelines, and are tailored according to tumor characteristics, molecular profile, and patient status. Multidisciplinary teams in tertiary centers facilitate evidence-based management, while ongoing efforts aim to expand access to targeted therapies and optimize care pathways. Insufficient training, limited knowledge, and suboptimal communication between primary care providers and specialists have been identified. Also, limited in-house molecular testing often leads to outsourcing, causing delays in targeted therapy and higher treatment costs. In this perspective article, we provide an overview of current practices and propose future perspectives for the screening, diagnosis, and management of CRC in the Gulf region, with the aim of aiding clinicians in making informed decisions, enhancing patient care, and establishing the cornerstone for future research.

Keywords: colorectal cancer, Gulf countries, screening, diagnosis, expert opinion

Introduction

Colorectal cancer (CRC) is the third most diagnosed cancer and the second leading cause of cancer-related deaths worldwide.¹ Approximately 1.93 million new cases and 0.94 million CRC-related deaths were reported in 2020, and global new cases are projected to reach 3.2 million by 2040.² In Gulf Cooperation Council (GCC) countries, CRC is one of the most common types of cancer, with an incidence rate of 9.9–15.9 per 100,000 people, the highest being in Qatar and the lowest in Oman.³ In the Kingdom of Saudi Arabia (KSA) and United Arab Emirates (UAE), CRC is the most common cancer among men and the third most common cancer among women after breast and thyroid cancer,^{4,5} while in Kuwait, Qatar, Bahrain, and Oman, CRC is the second most common cancer in both men and women.⁶⁻⁹

There has been an increase in the incidence of CRC among both males and females in a few GCC countries (Table 1). This may be attributed to changes in lifestyle, which include low physical activity, westernized dietary habits, increased consumption of red and processed meat, and habits such as smoking.^{10–14}

The increasing incidence of CRC underscores the need to assess current clinical practices in CRC management in the Gulf region, which are substantially different from those in Europe and North America. CRC screening programs are relatively recent and less prevalent, resulting in lower screening uptake and late-stage diagnoses. While some centers provide care that is consistent with international standards, others are subject to limitations in access to personalized medicine approaches and targeted therapies. As a result, the Gulf region's survival rates are generally lower than those of Europe and North America, where early detection through established screening programs and adherence to evidence-based treatment protocols significantly enhance outcomes.^{1,3,15}

Early diagnosis in CRC is critical for improving patient outcomes. International oncology societies such as the National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and the European Society for Medical Oncology (ESMO) have developed stratified clinical practice guidelines for CRC, incorporating regional adaptations.^{16–18} According to these guidelines, the diagnosis of CRC involves clinical assessment, colonoscopy, imaging, and molecular testing for key mutations (RAS, BRAF, MSI/MMR), which are essential for accurate staging and guiding personalized treatment strategies.^{16–18} Staging is based on histopathological evaluation and imaging to determine the extent of disease and inform management decisions.¹⁹ Management of CRC is tailored according to tumor characteristics, molecular profile, and patient status, and typically includes surgical resection for localized disease, adjuvant chemotherapy for high-risk or advanced stages, and targeted therapies or immunotherapy for metastatic cases.^{16–18} Multidisciplinary teams play a pivotal role in coordinating care, ensuring optimal treatment planning, and improving treatment outcomes.²⁰ Surveillance and follow-up are also recommended to monitor recurrence and manage the long-term effects of therapy.¹⁹

Despite regional adaptations in clinical practice guidelines, there is still a gap between the guideline recommendations and their implementation in everyday practice in some countries globally.²¹ It has been reported that in most developing countries, oncologists modify resource-stratified ASCO guidelines for CRC based on regional disparities and individual patient preferences.^{16,22} The first consensus recommendations for the management of advanced CRC in the Middle East and North Africa (MENA) region focusing on the epidemiology, screening, and management of CRC were recently published.²³ Also, NCCN guidelines for the MENA region have been recently published for colon cancer, and the first author (HOA) has been appointed as the chairperson of the CRC for the NCCN in the MENA region. However, there is still a scarcity of information concerning the challenges faced by clinicians regarding screening, diagnosis, and

Table 1 Incidence and Mortality Rates of CRC in GCC Countries

Country	2008–2012		2019–2020		Mortality Rate (per 100,000U)	
	Males	Females	Males	Females	Males	Females
Oman	Not available		11.2	7.7	4.5	3.7
Kuwait	11.5	11.6	13.1	11.9	5.3	4.7
UAE	Not available		13.1	6.5	5.1	4.3
Bahrain	16.9	11.7	13.7	14.6	5.7	4.8
KSA	12.6	11.7	16.1	10.9	5.5	4.5
Qatar	19.6	17.7	13.6	20.6	5.8	4.6

Notes: Cancer Incidence in Five Continents Vol. XI (2008–2012); Cancer incidence in UAE Annual report of the UAE National Cancer Registry-2019; The global cancer observatory, International Agency for Cancer Research, WHO 2020, National Cancer Registries of GCC Countries. (2022). Annual Cancer Reports for GCC Countries. Ministries of Health of Saudi Arabia, UAE, Qatar, Bahrain, Kuwait, and Oman. Retrieved from respective national health website.

Abbreviations: CRC, colorectal cancer; GCC, Gulf Corporation Council; KSA, Kingdom of Saudi Arabia; UAE, United Arab Emirates.

management, and there is also a need to bridge gaps between primary and tertiary care physicians in terms of CRC management in the Gulf region.

Contrary to this, Europe and North America have established CRC management practices that are characterized by high compliance rates for screening. This is a result of the robust public health systems and awareness campaigns. Multidisciplinary teams, sophisticated technologies, and standardized diagnostic and treatment approaches are beneficial to these regions, as they provide a patient-centered and coordinated approach to care. The prevalence of personalized medicine, which encompasses molecular profiling and targeted therapies, is increasing, resulting in improved 5-year survival rates. Nevertheless, both regions encounter obstacles, including the management of healthcare expenses and the resolution of socio-economic disparities. To reduce the disparity in CRC outcomes between the Gulf region and Western countries, the primary objectives should be to enhance adherence to international guidelines, invest in healthcare infrastructure and training, and expand screening programs.^{1,3,15}

To address current evidence gaps in practice, expert opinions were gathered from key opinion leaders in the region. This article aims to summarize these expert opinions, help clinicians make informed decisions, and guide the management of CRC in the GCC region.

Methods

A discussion guide ([Supplemental material 1](#)) was developed based secondary desk research to gain more insights from the experts in the GCC region on the identified evidence gaps. Opinions were gathered from experts in the GCC region through face-to-face or telephonic interviews. The experts included medical oncologists, radiation oncologists, surgical oncologists, gastroenterologists, pathologists, and radiologists with expertise in CRC. They provided their input on current practices for the screening, diagnosis, and management of CRC in the GCC region and put forward recommendations to improve the overall care of patients in the region. The selection of the experts is based on the local knowledge of the experts who treat CRC in the region. These experts are all known in the region for their expertise and interest in the treatment of CRC.

Secondary desk research was conducted using public electronic databases such as PubMed/MEDLINE (“Colorectal Neoplasms”[Mesh], “Gulf Cooperation Council” OR GCC OR “Kingdom of Saudi Arabia” OR KSA OR “United Arab Emirates” OR UAE OR Kuwait OR Qatar OR Bahrain OR Oman OR “Middle East and North Africa” OR MENA, “Epidemiology”[Mesh] OR “Incidence”[Mesh], “Screening”[Mesh] OR “Diagnosis”[Mesh] OR “Management”[Mesh] OR “Treatment” OR “Clinical Practice Guidelines” OR “Healthcare Disparities”[Mesh] OR “Survival Rate”[Mesh] OR “Personalized Medicine” OR “Targeted Therapies”) and Google Scholar to understand the current landscape and evidence gaps for CRC management in the GCC region.

Results

Screening Methods for CRC

Screening is a critical step in the management of CRC, as early detection can aid in early treatment initiation. Over the last two decades, there has been a paradigm shift in screening methods for CRC. Early detection and removal of premalignant lesions, such as adenomatous polyps, may prevent the development of CRC.²⁴ Evidence from community-based populations in urban areas in the US indicates that increased CRC screening is associated with a decrease in CRC incidence (ranging from 2.8% to 25.5%) and mortality (ranging from 2.9% to 52.4%) rates.^{25,26} Additionally, early detection of CRC can reduce the economic burden associated with treatment.²⁷

Common screening methods for CRC include fecal occult blood testing (FOBT) (guaiac-based [gFOBT] or fecal immunochemical test [FIT]), flexible sigmoidoscopy (FS), colonoscopy, double-contrast barium enema, computed tomography (CT) colonography, video capsule colonoscopy, and stool DNA (sDNA) testing.²⁸ Currently, most developed countries have some kind of screening program for CRC.²⁹ In the United States of America (US), the US Preventive Services Task Force (USPSTF) recommends annual high-sensitivity guaiac FOBT (gFOBT) or FIT in patients aged ≥ 45 years; sDNA-FIT every one to three years; CT colonography every five years; FS every five years; or colonoscopy every ten years.³⁰ Similarly, European guidelines recommend gFOBT and FIT for population-based screening programs.³¹

Bahrain was the first country in the GCC region to implement CRC screening in 2010, followed by the UAE, Kuwait, and Qatar in 2013, 2014, and 2017 respectively.³²

Published data suggest that CRC screening modalities vary between countries across the Gulf region. A study conducted in the KSA reported stool FIT as the most preferred screening modality for the general population, followed by stool FOBT and colonoscopy.³³ A cross-sectional survey assessing CRC risk awareness and screening uptake in the UAE described colonoscopy as the preferred screening method, followed by FOBT and sigmoidoscopy.²⁴ Stool-based screening methods are preferred for the general population, as they are less invasive and distressing to patients while being more economical compared with other modalities.¹⁰ Screening practices for CRC among GCC countries as per 2017 World Health Organization records are elaborated in Table 2.³¹

Although screening programs have been established in the Gulf region, screening uptake remains very low.²⁴ Studies conducted across different GCC countries have reported suboptimal knowledge among participants regarding risk factors, screening tests, symptoms, and an overall lack of awareness of CRC.^{24,34–36} A combination of cultural, economic, and logistical factors influences the barriers to CRC screening adoption in the Gulf region. Many individuals are deterred from engaging in screening due to cultural factors such as stigma, embarrassment, and gender-specific issues. This is especially true in conservative societies where procedures such as colonoscopies are seen as invasive, uncomfortable, or inappropriate. Economically, the high cost of CRC screening procedures, such as colonoscopies and advanced imaging tests, can be a significant burden, particularly for those without comprehensive health insurance coverage. In the Gulf region, while healthcare services are often subsidized or free for citizens, expatriates—who make up a large portion of the population—frequently rely on private insurance or out-of-pocket payments, which may not fully cover preventive services such as CRC screening. Additionally, lower-income groups, including many migrant workers, may lack the financial resources to prioritize such screenings, especially when faced with competing basic living expenses. This economic disparity creates a significant barrier to early detection and timely intervention, ultimately impacting overall health outcomes in the region. Expanding insurance coverage to include preventive care and providing subsidies or financial assistance for screening could help reduce these economic barriers and promote wider participation in CRC screening programs. Logistically, uneven access to advanced screening facilities, particularly in rural areas, combined with a shortage of specialized healthcare professionals, long waiting times, and inadequate national screening programs, further hinders the effective implementation and uptake of CRC screening across the region.^{11,37–40}

Currently, the application of artificial intelligence (AI) in CRC screening is gaining great interest, as bioinformatics tools coupled with traditional screening techniques such as colonoscopy can identify more CRC cases. A multicenter randomized control trial conducted using AI-assisted colonoscopy in asymptomatic patients reported significantly improved adenoma detection rates (ADR) for both expert and nonexpert attending endoscopists.⁴¹ Further, a recent meta-analysis that included 11 clinical trials comprising 6856 participants has also reported significantly improved polyp

Table 2 Practice Considerations for CRC Screening in GCC Countries

Country	Start Year	Target Age Range (Years)	Screening Interval (Years)	Recommended Screening Test
Bahrain	2010	50–90	1	FIT
UAE	2013	40–75	2 (FIT) 10 (Colonoscopy)	FIT/Colonoscopy
Kuwait	2014	≥50	2	FIT
Qatar	2016	50–74	1	FIT
KSA	2017	45–75	1 (FIT) 2 (Colonoscopy)*	FIT/Colonoscopy*
Oman	Data not available			

Notes: IARC Handbooks of Cancer Prevention, Volume 17. * Source: Benard et al, 2018.²⁸

Abbreviations: CRC, colorectal cancer; GCC, Gulf Corporation Council; FIT, fecal immunochemical test; KSA, Kingdom of Saudi Arabia; UAE, United Arab Emirates.

detection rate (odds ratio [OR] = 1.89, $p < 0.0001$) and ADR (OR = 1.51, $p = 0.003$) with AI-supported colonoscopy compared with standard colonoscopy.⁴² Currently, a clinical trial using AI is ongoing in the UAE and the US to identify patterns of cell-free biomarkers in blood for early detection of CRC.⁴³ Validation and inclusion of AI-based techniques in GCC screening programs may aid in the early detection of CRC while lowering misdiagnosis or missed diagnoses. Additionally, there has been extensive research to identify appropriate biomarkers for CRC screening. Blood-based markers and liquid biopsy are being developed to aid in more accurate and less invasive screening techniques.^{44,45} In July 2024 the Food and Drug Administration (FDA)-approved Guardant Shield™ which was a qualitative, in vitro diagnostic test intended to detect CRC derived alterations in cell-free DNA from blood, the FDA-approval for use in adults age 45 years and older who are at average risk of CRC. This is the first FDA-approved blood test for primary CRC screening.

Screening Considerations

Age

Age is one of the most important risk factors for CRC, with incidence rates increasing with age.⁴⁶ However, several studies have reported increasing CRC incidence among younger patients globally, as well as in the Gulf region.^{47–51} Considering the declining age of incidence, the NCCN and the USPSTF amended their guidelines and now recommend that all adults aged ≥ 45 years be screened for CRC, even in the absence of risk factors.^{30,52} However, guidelines in European countries recommend CRC screening only for individuals aged 50–74 years.⁵³ Based on the results of retrospective studies, the age for CRC screening has been lowered to 45 years in most GCC countries.^{10,15} However, the Health Authority of Abu Dhabi and a study from Bahrain recommend CRC screening for all patients aged ≥ 40 years.^{54,55}

The exact causes for the current trend of a young age of incidence remain unclear, and several factors, such as the adoption of westernized lifestyles and modifications in dietary habits with a lack of physical activity, leading to obesity, have been implicated in the increased prevalence of CRC in the younger population in the Gulf region.^{10,13,56} According to the 2019 annual cancer incidence report for the UAE, the highest frequency of malignant cases of cancer was noted in the 40–44 years age group (12.0%), followed by the 45–49 years age group (11.6%), and the number of cases gradually declined with age.⁵ The median age at diagnosis of CRC in the UAE has been reported to be 51 years. Analysis of data from the 2015 UAE National Cancer Registry revealed the onset of CRC below the age of 50 in 23.4% of UAE nationals and in 41.9% of non-UAE nationals.⁵⁷

Presence of Precancerous Conditions

Consanguineous marriage, common in Gulf countries, increases the likelihood of homozygosity for recessive mutations, raising the risk for hereditary CRC syndromes such as MUTYH-associated polyposis and other autosomal recessive conditions.⁵⁸ Genetic testing is especially important in these populations for early identification and management of syndromes such as familial adenomatous polyposis and Lynch syndrome, which are characterized by multiple adenomatous polyps and a high risk of CRC.^{59,60} Guidelines from the NCCN and ESMO recommend genetic counseling and testing for individuals with multiple polyps, early-onset CRC, or a suggestive family history, enabling timely surveillance and preventive interventions.^{20,61,62}

Evidence from literature reports a higher risk of CRC among patients with ulcerative colitis, Crohn's disease, and inflammatory bowel disease (IBD) compared with the general population,^{63,64} requiring patients with these conditions to be aware and consider screening for CRC. The recent systematic review and meta-analysis study by Mosli et al reported the rising incidence of IBD in the Middle East region; however, there are insufficient data on IBD leading to the development of CRC in GCC countries.⁶⁵ In patients with IBD, early symptoms of CRC often overlap with IBD symptoms and cannot be reliably distinguished. Therefore, screening based on international guidelines is recommended rather than waiting for symptoms. Colonoscopy should begin 8 years after IBD diagnosis, especially in cases of extensive colitis, and be repeated at regular intervals, depending on risk factors and findings.^{16,66}

Based on published evidence and observations from clinical practice, the expert panel recommended screening for all adults aged ≥ 45 years, except patients with Lynch syndrome, in whom screening should be initiated at the age of 25

years. To improve screening uptake, the experts recommended bridging the gap between primary and tertiary care physicians by conducting periodic educational programs pertaining to the identification of high-risk patients and appropriate screening referrals. In Bahrain, awareness of the importance of screening has been created by conducting screening campaigns with public figures and using social media platforms. Similar activities can be considered by other GCC countries to raise awareness of CRC screening. Screening recommendations for CRC in the Gulf region are outlined in [Box 1](#).

Diagnostic Tests for CRC

Imaging techniques play a crucial role in clinical decision-making during the management of CRC. The initial diagnostic approach for suspected CRC begins with colonoscopy, which is the gold standard for direct visualization, biopsy, and removal of premalignant polyps.^{16,66} Colonoscopy not only confirms the diagnosis but also allows for histopathological evaluation.^{16,66} In cases where colonoscopy is incomplete or contraindicated, alternative modalities such as CT colonography or FS may be considered, especially in centers where these technologies are available.^{16,66}

For patients with unclear or indeterminate findings on colonoscopy, further evaluation is warranted.⁶⁷ Contrast-enhanced CT scans of the chest, abdomen, and pelvis are routinely used to assess local and distant disease spread.⁶⁷ For rectal cancer, MRI is preferred for its superior soft tissue resolution, enabling accurate assessment of tumor depth, mesorectal fascia involvement, and lymph node status.⁶⁷ Endoscopic ultrasound (EUS) is particularly useful for early-stage rectal tumors to evaluate depth of invasion and nodal involvement and is recommended in centers equipped with this technology.⁶⁷

CRC staging is based on the TNM classification and integrates findings from colonoscopy, histopathology, and cross-sectional imaging.^{16,66,67} For localized (Stages I–II) disease, colonoscopy and biopsy are followed by CT scans to rule out metastatic spread. In rectal cancer (Stages I–III), pelvic MRI is the standard for local staging, while EUS may be used for superficial tumors.^{16,66,67} For advanced or metastatic (Stage IV) disease, CT scans remain the mainstay for detecting distant metastases, and positron emission tomography (PET) scans may be utilized in select cases, such as when metastatic disease is suspected but not confirmed by conventional imaging, or for evaluating equivocal lesions.^{16,66,67}

Carcinoembryonic antigen (CEA) plays a significant role in the management of CRC, both at baseline and during follow-up.⁶⁸ Preoperative CEA levels are routinely measured, as elevated values (>5 ng/mL) are associated with a higher risk of recurrence and metastatic disease. However, normalization of CEA levels after curative resection is linked to recurrence-free survival rates comparable with those with normal preoperative CEA levels.⁶⁸ Postoperative CEA monitoring is even more prognostically valuable. Persistently elevated levels are independently associated with shorter recurrence-free survival and earlier disease recurrence.⁶⁸ Current guidelines recommend serial CEA testing every 3–6 months for the first two years, and every 6 months thereafter up to five years for patients with stages II–III disease.⁶⁸

Although the data on exact imaging and other facilities available in GCC countries are limited, in most GCC countries, advanced imaging facilities such as CT, MRI, Gamma cameras, PET, MRI, and laboratory testing facilities (such as molecular testing and genetic testing) are available, both in privately run clinics and in tertiary hospitals.^{69,70}

Countries such as the UAE, Qatar, and Saudi Arabia are at the forefront of providing comprehensive diagnostic services, including colonoscopy, CT colonography, MRI, PET scans, and molecular testing. Additionally, these countries

Box 1 Expert Recommendations for CRC Screening in Gulf Region

1. All patients aged ≥ 45 years should be screened for CRC. Patients with a family history of CRC and Lynch syndrome should be advised to undergo screening at a younger age of 25 years. Some countries, such as the UAE, advise CRC screening even in patients aged 40 years.
2. Patients with IBD, Crohn's disease, ulcerative colitis, and obesity/overweight should be screened regularly for any symptoms of CRC.
3. As FIT is not routinely used in some GCC countries, colonoscopy is recommended as the gold-standard screening and diagnostic tool for CRC. FIT is also recommended in some GCC countries based on patient conditions.
4. To improve CRC awareness among the general population, the experts recommended the implementation of national screening campaigns with general population participation and through social media campaigns.
5. The experts recommend collaboration between primary care physicians and specialists to implement screening and early diagnosis of CRC cases.

are incorporating advanced technologies such as AI and digital health solutions into their CRC screening programs, resulting in notable improvements in detection rates and a decrease in missed diagnoses. AI-enhanced colonoscopy is now being investigated in clinical trials to enhance ADR and minimize polyp detection mistakes. Moreover, there is an increasing interest in the utilization of non-invasive screening techniques such as liquid biopsies and blood-based biomarkers. These technologies provide less intrusive and perhaps more readily available options compared to the conventional colonoscopy. Nevertheless, whereas urban centers have greater accessibility to modern techniques, rural and isolated locations encounter substantial gaps in access. Moreover, nations such as Kuwait, Bahrain, and Oman continue to have limited general availability of these newer techniques.^{60,71–73}

In order to tackle these challenges and improve the management of CRC, a number of Gulf nations are making significant investments in the expansion of their healthcare infrastructure and the incorporation of new technology. These efforts are being carried out as part of larger national development strategies, such as Saudi Vision 2030. This involves expanding the quantity of specialist diagnostic facilities and integrating cutting-edge technologies such as AI-based diagnostic tools and liquid biopsy testing into standard healthcare practices. Furthermore, there is a growing emphasis on using molecular and genetic tests, such as RAS, BRAF, and MSI/MMR mutations, to provide more customized and efficient treatment approaches. This represents a transition toward a more individualized approach to therapy in the area.

Multidisciplinary Approach to CRC Management

To ensure timely and optimal evidence-based management of CRC, implementing a multidisciplinary approach to meet the unique needs of individual patients is imperative.⁷⁴ Multidisciplinary teams (MDTs) play a pivotal role in managing and improving patient care pathways. Additionally, specialized CRC MDTs play an important role in the management of patients with metastatic CRC, such as those with liver and lung metastatic lesions.⁷⁵

Available data demonstrate improved survival with CRC management through MDTs.⁷⁶ Currently, tertiary hospitals in the GCC region have dedicated MDTs for treating CRCs.^{15,69,77} The experts across the Gulf region highlighted that tertiary hospitals have established MDTs for accurate tumor staging and treatment planning to meet the needs of individual patients. In Kuwait, there are MDTs in place for CRC that include hepatobiliary surgeons, oncosurgeons, radiation oncologists, pathologists, nutritionists, medical oncologists, and intervention radiologists.

Treatment of CRC

Early-Stage Disease

As there are limited randomized trials reporting treatment outcomes specific to the GCC region, the Gulf region has adopted the NCCN Clinical Practice Guidelines in Oncology for the management of CRC.⁷⁸ Several factors that guide the planning of treatment for CRC include tumor characteristics, the patient's fitness for treatment (assessment of performance status using the Eastern Cooperative Oncology Group scale), the patient's overall health condition, the patient's molecular profile, and tumor location.⁷⁹

Anatomically, the colon and rectum are different in localization, blood supply, drainage, and innervation, and hence there are differences in surgical approaches and treatment outcomes. The current standard treatment for early-stage (stages I–IIIC) colon cancer consists of resection of the primary tumor either by laparoscopy or open resection along with the regional lymph nodes.^{66,80} Patients with high-risk stages II and III colon cancer have a survival benefit with adjuvant chemotherapy following surgery.⁸¹ Surgery following the principle of total mesorectal excision (TME) is the primary treatment modality for early rectal cancer.⁶⁶ Surgery following the TME approach has been reported to minimize local-region recurrence. Further, neoadjuvant therapy (chemotherapy and chemoradiotherapy) improves the resection rate, the rate of sphincter preservation, and prolongs disease-free survival in patients with rectal cancer.^{82,83} Total neoadjuvant therapy (TNT) is a new multimodal treatment strategy for locally advanced rectal cancer that administers both radiation and systemic therapy before surgical excision. Several trials have demonstrated the favorable effects of TNT in terms of superior disease-free survival, pathologic complete response, a higher number of patients completing chemotherapy, lower disease-related treatment failure and distant metastatic disease.⁸⁴ According to the experts, the criteria for administering neoadjuvant therapy vary between centers. The treatment choice is based on the tumor location, presence of enlarged suspicious lymph nodes, positive extramural venous invasion, circumferential resection margin, and T3 and

T4 stages of disease. Most guidelines recommend TNT, including neoadjuvant radiotherapy and chemotherapy, in high-risk or low-lying rectal cancer patients.⁸⁵ In Gulf countries such as the UAE, oncologists occasionally see patients with rectal cancers who were operated on upfront without neoadjuvant therapy. Most of these cases are treated in small non-oncology centers, which reflects the need to increase awareness about the importance of MDT among community surgeons.

Molecular Testing for CRC

Molecular testing is an essential component in CRC management, particularly in metastatic settings. Genetic mutations conferring benefit or lack of benefit to some antineoplastic agents have been reported; therefore, molecular testing for *RAS* and *BRAF* mutations has become part of the standard of care in mCRC.⁸⁶ Additionally, there have been encouraging reports that microsatellite instability/mismatch repair (MSI/MMR) status could inform the response to immunotherapy in CRC.⁸⁷ *RAS* mutations are known drivers of CRC tumorigenesis and are estimated to occur in approximately 35%–45% of cases globally.^{88,89} The common genetic mutations reported in CRC patients in the Middle Eastern region include *RAS* (38.5%), *BRAF* (12.9%), and *PI3KCA* (11.1%).⁹⁰ A retrospective study conducted at King Abdulaziz University Hospital, Jeddah, KSA reported *KRAS* (45.2%), *NRAS* (2.2%), and *BRAF* (2.2%) to be the most prevalent mutations and *KRAS* p. G12D to be the most common variant in Saudi patients with CRC.⁹¹ *KRAS* G12C mutations associated with shorter survival are reported in 3%–4% of patients with mCRC.⁹² The experts highlighted that nearly 2% of patients with mCRC have *KRAS* G12C mutations in Kuwait, which are evaluated as a part of the comprehensive molecular testing panel in Kuwait.

According to the ASCO and ESMO guidelines, patients with mCRC considered for anti-EGFR therapy should undergo *RAS* mutational testing, including *KRAS* and *NRAS* codons 12 and 13 of exon 2, 59 and 61 of exon 3, and 117 and 146 of exon 4.^{20,93} Usually, in the Gulf region, molecular testing has been limited to the evaluation of *KRAS* and *BRAF*, although MSI/MMR are now increasingly done for most CRC patients. *RAS* testing is the standard of care for all newly diagnosed, histologically proven mCRC.^{94,95} *BRAF* mutations are negative prognostic biomarkers found in 8%–12% of mCRC patients.²⁰ A study with 500 patients from Saudi Arabia has reported a frequency rate of 30.1% and 2.4% for *KRAS* and *BRAF* mutations, respectively.⁷² Another retrospective study of Arab patients from Gulf countries treated in the US reported the frequency of *KRAS* to be higher, followed by *NRAS* and *BRAF*.⁷¹

Other potential biomarkers for mCRC include human epidermal growth factor receptor (*HER2*) and neurotrophic tyrosine receptor kinase (*NTRK*). *HER2* overexpression is present in about 3%–5% of cases of mCRC; a few clinical trials are currently investigating various anti-HER-2 therapies in mCRC.^{96–99} *NTRK*-fusion-positive CRCs are rare, exhibiting a high tumor mutation burden, and are common among females and right-sided primary tumor locations.¹⁰⁰

The expediency of reporting biomarker results for CRC is important for patient management. ASCO guidelines recommend a turnaround time of ten working days from the receipt of the specimen at the laboratory to the disclosure of biomarker results to the treating physician.⁹³ Studies have reported that *ctDNA* genotyping accurately identifies all the biomarkers associated with mCRC;^{101,102} however, *ctDNA* has been used only in clinical trials.

There is a paucity of literature on molecular testing in the Gulf region, as well as a lack of regional recommendations. Based on their clinical experience and international guidelines, the experts recommended molecular testing for all mCRC patients upon diagnosis. *MSI/MMR* identification was recommended in early CRC cases, while *RAS* and *BRAF* were advised for advanced CRC. Expert recommendations regarding molecular testing for the Gulf region are elaborated in Box 2.

Advanced-Stage Disease

As per consensus recommendations from MENA countries, first-line treatments for patients with mCRC include FOLFOX or FOLFIRI combined with anti-EGFR or anti-VEGF antibodies, as appropriate.²³ The effectiveness of anti-EGFR and anti-VEGF treatments combined with FOLFIRI or FOLFOX is based on tumor sidedness and the tumor burden.¹⁰³ In the presence of a *BRAF* mutation or in those with right-sided disease, FOLFIRINOX/FOLFOX in combination with bevacizumab is recommended in the first-line setting.²³ A combination of encorafenib and cetuximab has shown favorable efficacy and safety in *BRAF* (V600E)-mutated mCRC patients who had disease progression after previous lines of therapy.^{104,105} Tipiracil/

Box 2 Expert Recommendations on Molecular Testing in Gulf Region

1. Molecular testing should be done for all mCRC patients upon diagnosis.
2. For metastatic cases, the recommended mutations to be tested include *KRAS*, *HER2*, *BRAF*, and *MSI/MMR*. In some cases, *KRAS* G12C is advisable.
3. For all early CRC cases, testing of *MSI/MMR* should be performed.
4. As most samples are sent out of the country for molecular testing and a delay in the report turnaround is expected, the experts recommend setting up testing facilities within each GCC country to initiate earlier treatment.
5. Molecular testing is recommended in cases of early-stage CRC progressing to the metastatic stage. In some cases, molecular testing is advised for refractory mCRC.

trifluridine or regorafenib is recommended in third-line therapy for mCRC.²⁰ Further, the combination of tipiracil/trifluridine plus bevacizumab has been recently approved by the FDA for mCRC based on the results of the SUNLIGHT trial, which demonstrated longer overall survival and progression-free survival among patients with refractory mCRC.¹⁰⁶ A retrospective study by Aljubran et al in the KSA among mCRC patients receiving regorafenib reported a median progression-free survival and overall survival of 2.8 and 8 months, respectively. The authors reported that efficacy parameters were higher than those reported in the pivotal CORRECT and CONCUR clinical trials and concluded that performance status was an important prognostic factor among patients treated with regorafenib.¹⁰⁷

The experts recommended NCCN as a commonly used guideline for the treatment of CRC. Additionally, the NCCN guidelines for the MENA region have been recently published to aid clinicians in managing CRC. The experts emphasized the variability in treatment options based on tumor characteristics and sidedness, the molecular profile of the tumor, and patients' performance status and comorbidities. The experts also advocated treatment optimization by increasing disease awareness, expanding accessibility to molecular targeted therapy, and increasing the number of subspecialty units within the Gulf region to improve treatment outcomes. The treatment recommendations for the Gulf region are outlined in [Box 3](#).

Box 3 Expert Recommendations on Treatment Guidelines for CRC in Gulf Region

1. Treatment should be based on tumor characteristics, tumor sidedness, molecular profile, patients' performance status, comorbidities, and patients' preferences.
2. Adjuvant therapy is advised for stage 3 and high-risk stage 2 disease. Based on the revised NCCN guidelines, the experts recommended that adjuvant treatment be continued for 3–6 months, depending on risk stratification.
3. Chemotherapy with doublet therapy (FOLFOX or FOLFIRI) or triplet FOLFOXIRI is recommended as the first line of treatment based on tumor characteristics, tumor sidedness, molecular profile, patients' performance status, and comorbidities.
4. In the case of *KRAS* wt and *BRAF* wt patients, anti-EGFR + chemotherapy is advised for left-sided tumor and anti-VEGF + chemotherapy for right-sided tumors.
5. Targeted therapy for patients with *BRAF* and *HER-2* mutations is recommended in the second- and third-line settings. For patients with no actionable mutations, regorafenib or tipiracil/trifluridine is recommended in the third line (regorafenib, or regorafenib + nivolumab, lonsurf/bevacizumab).
6. For patients with high MSI and deficient MMR, immune therapy is recommended for locally unresectable CRC as neoadjuvant treatment and for metastatic CRC as a palliative first-line of treatment.
7. Treatment of mCRC patients with liver metastasis should be individualized and managed by a multidisciplinary team with expertise in managing mCRC.
8. Based on NCCN guidelines for the MENA edition, the experts recommend rechallenging anti-EGFR monotherapy in positive ctDNA assays after initial treatment with an EGFR agent and in CRC progressing after the last anti-EGFR-free regimen.

Follow-Up

1. Post-treatment surveillance should include following up with patients with early CRC for up to five years. For the first 2–3 years, follow-up scans and colonoscopy are advised. Lab investigations, including a complete blood count, liver profile, and tumor markers, should be performed at every visit.
2. Patients with stages 2–3 CRC receiving adjuvant therapy should be referred to surveillance clinics every three months for the first two years, every four months in the third year, and every six months from the fourth year onward.

In complicated CRC cases presenting with intestinal obstruction or perforation, urgent surgical intervention is often necessary.^{108,109} Treatment options depend on patient stability, tumor location, and disease extent, and may include resection with primary anastomosis, resection with a protective stoma, or diversion procedures such as loop colostomy or ileostomy to relieve obstruction and stabilize the patient before definitive surgery.^{108–110} In cases of perforation, damage control surgery with fecal diversion and peritoneal lavage may be required to manage sepsis.^{108–110} Protective stomas, such as loop ileostomies or colostomies, are commonly used in colorectal surgery to divert fecal flow and reduce pressure on a new anastomosis.^{108–110} Their primary role is to minimize the impact of anastomotic leaks, which are a major source of postoperative morbidity. While they do not prevent leaks entirely, they reduce clinical severity and support healing.^{108–110} Protective stomas are especially recommended in high-risk patients, including those with poor nutrition, immunosuppression, or low pelvic anastomoses.^{108–110}

Roadmap for Future

In conservative societies, discussions about cancer and related tests are considered sensitive, and there are several practical challenges associated with the implementation of recommendations for CRC screening and management in the Gulf region. These challenges include low public awareness and education about CRC, cultural stigma, and discomfort with screening procedures such as colonoscopies. Preventive care is financially inaccessible due to the high costs of screening and limited insurance coverage for expatriates and lower-income groups, which are also significant factors. The adoption of screening is further impeded by logistical issues, including a shortage of specialized healthcare professionals and uneven access to advanced screening facilities, particularly in rural areas. Furthermore, the integration of advanced technologies such as AI into extant healthcare systems necessitates a substantial investment in data infrastructure and training. To guarantee timely referrals and appropriate management, it is also necessary to establish effective coordination between primary and tertiary care providers.

Further critical areas of research for improving CRC management in the Gulf region include understanding the unique genetic and molecular profiles of CRC patients, such as the prevalence of specific mutations such as RAS, BRAF, and MSI/MMR, which can inform more tailored and effective treatment strategies. Research is also needed to optimize screening methodologies by focusing on non-invasive, cost-effective options such as stool DNA tests and blood-based biomarkers that are better suited to the Gulf population's needs. Health systems research that evaluates the effectiveness of various CRC screening programs, patient pathways, and the role of multidisciplinary teams can help enhance healthcare delivery and coordination. Conducting public health and behavioral research to assess knowledge, attitudes, and practices regarding CRC screening will facilitate the development of targeted awareness campaigns and strategic interventions.

Vaccines represent a promising area of research in CRC, with several candidates currently undergoing clinical trials. For example, the ELI-002 peptide vaccine targets KRAS mutations and has demonstrated promising immune responses in early-phase trials (NCT04853017).¹¹¹ BioNTech's individualized mRNA vaccine (BNT122) is in Phase II trials for high-risk patients with CRC, designed to encode patient-specific neoantigens and prevent relapse after surgery and chemotherapy.¹¹² Dendritic cell-based vaccines are also under investigation, with studies showing a tendency toward fewer and later relapses in patients with CRC receiving these vaccines after metastasis resection.¹¹³ Although none have regulatory approval yet, these trials demonstrate the potential of vaccines for CRC treatment and relapse prevention.

Lifestyle modification is an integral part of survivorship care for patients with CRC. The NCCN Survivorship Guidelines (Version 1.2024) recommend regular physical activity (at least 150 minutes of moderate exercise per week), a diet rich in vegetables, fruits, and whole grains (while limiting red and processed meats and alcohol), and maintaining a healthy body weight.¹¹⁴ Smoking cessation and adequate sleep are also advised. These recommendations are supported by the American Cancer Society and World Cancer Research Fund, which emphasize that such changes can reduce recurrence risk and improve overall quality of life.^{115,116} In GCC countries, diet and lifestyle play a key role in CRC prevention. Diets that are high in fruits, vegetables, and dietary fiber have been shown to confer protective benefits, whereas elevated consumption of red meat, refined carbohydrates, and certain dairy products is associated with increased risk. Engaging in regular physical activity is associated with a reduced risk of CRC, while sedentary behavior is linked to

an increased risk. The impact of smoking in Gulf populations is unclear, although it is linked to a higher CRC risk. Therefore, promoting healthy diets and active lifestyles may reduce the incidence of CRC in the region.¹¹⁷

In order to tackle these difficulties, it is crucial to promote cooperation among regions, exchange successful strategies, and standardize protocols for the management of CRC. It is essential to implement multi-level interventions, which involve policy changes, strengthening healthcare systems, forming public-private partnerships, and engaging the community. Enhancing the involvement of healthcare professionals through ongoing education and training, augmenting financial resources for CRC research, and developing public awareness initiatives that are specifically adapted to the local culture can greatly enhance the outcomes of CRC management in the Gulf region.

To promote regional cooperation, a Gulf Cancer Research Consortium can be formed to facilitate collaboration among experts from various nations. This consortium would focus on conducting joint studies, exchanging data, and creating uniform guidelines. Regular regional conferences, workshops, and collaborative research endeavors can facilitate the exchange of knowledge and the development of skills. Using digital platforms to share data and establish registries for patients with CRC across the GCC countries would enhance collaborative research and enhance the management of CRC in the area.

Conclusion

Considering the increasing prevalence of CRC in the Gulf region in the last decade, it is necessary to increase disease awareness and improve screening acceptance among the general population. Periodic educational programs are recommended, especially for primary health care professionals, to help identify patients with a high-risk of CRC and appropriately refer them to tertiary care, thereby enabling early diagnosis and treatment initiation. More research is needed among the GCC population to understand the molecular differences between the GCC and Western populations. Additionally, the establishment of facilities for molecular testing within each region may substantially enhance the diagnosis and management of CRC.

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Author Contributions

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