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Artificial Intelligence in Colon Cancer: Advances, Challenges, and Future Perspectives

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Rezumat

Inteligența artificială în cancerul de colon: progrese, provocări și perspective de viitor

Cancerul colorectal (CCR) rămâne o problemă majoră de sănătate publică, cu incidență în creştere la vârste tinere şi mortalitate ridicată. Inteligența artificială (IA) schimbă semnificativ îngrijirea pacienților, îmbunătățind precizia şi eficiența diagnosticului, tratamentului şi a monitorizării. În endoscopie, sistemele IA cresc rata de detecție a adenoamelor şi ajută la caracterizarea rapidă a leziunilor. Anatomia patologică, beneficiaza de analiza digitală a lamelor care poate susține triajul automat, predicția instabilității microsatelitare şi estimarea riscului prognostic, uneori peste performanța stadializării TNM. În radiologie, IA contribuie la detectarea şi stadializarea leziunilor şi poate sugera profiluri moleculare prin radiomică. Prin integrarea informațiilor din histopatologie, imagistică şi analize biologice avansate, IA poate rafina deciziile terapeutice, prezice răspunsul la tratamentul neoadjuvant şi sprijini chirurgia prin recunoaştere anatomică şi estimarea riscului de complicații. Totuşi, implementarea largă este limitată de variația datelor, necesitatea validării externe, interpretabilitate şi cerințe de reglementare. Odată depăşite aceste obstacole, IA are potențialul de a deveni un pilon al oncologiei de precizie în cancerul colorectal.

Cuvinte cheie: inteligență artificială, cancer colorectal, screening, anatomie patologică digitală, chirurgie minim invazivă

Abstract
Colorectal cancer (CRC) remains a significant global health challenge, with rising incidence in younger populations and high mortality. Artificial intelligence (AI) is transforming CRC care, enhancing accuracy and efficiency across diagnostic, therapeutic, and follow-up stages. In endoscopy, computer-aided detection (CADe) systems increase adenoma detection rates by 25–50%, while computer-aided diagnosis (CADx) supports real-time lesion characterization. In pathology, AI applied to whole-slide imaging enables automated triage, in silico microsatellite instability prediction, and prognostic risk stratification, often outperforming TNM staging. Radiology benefits from AI-driven lesion detection, staging, and radiomic "virtual biopsy" for molecular profiling (e.g., KRAS, MSI). AI-based treatment planning integrates histopathology, imaging, and multi-omics to refine chemotherapy indications, predict neoadjuvant response, and identify novel therapeutic targets. In surgery, AI-enhanced robotic platforms enable real-time anatomical recognition, perfusion assessment, and complication risk prediction, improving intraoperative safety. Prognostic modeling using multimodal datasets offers superior survival and recurrence predictions, while AI-driven quality-of-life forecasting and patient-reported outcome monitoring facilitate personalized survivorship care. Challenges to widespread adoption include data heterogeneity, external validation gaps, interpretability, and regulatory compliance. Advances in multimodal AI and federated learning may overcome these barriers. With rigorous evaluation, AI is poised to become a cornerstone of precision oncology in CRC, improving outcomes and optimizing care delivery.

Keywords: artificial intelligence, colon cancer, screening, digital pathology, precision oncology, minimal invasive surgery

Introduction

Colorectal cancer (CRC) remains a major global health burden, with approximately 1.9 million new cases and 930,000 deaths reported in 2020 (1). Projections suggest that it could rise to over 3 million cases and 1.6 million deaths annually by 2040, if current trends persist (1). Once concentrated in high-income countries, CRC incidence is now increasing rapidly in low- and middle-income regions, driven by urbanization, aging population, and lifestyle changes including Westernized diets (1). Notably, early-onset colorectal cancer (CRC), defined as CRC diagnosed in individuals under the age of 50, is increasing at an alarming rate, with projections indicating it could account for 11% of all cases by 2030 (2). This shift, though not fully understood, is associated with modifiable risk factors such as obesity, ultra-processed food intake, alcohol use, physical inactivity, and gut microbiome alterations (2).

Colonoscopy remains the cornerstone of colon cancer screening but has limitations, with up to 25% of adenomas – especially flat or proximal lesions – missed during examination (3,4,5). These diagnostic gaps highlight the need for improved detection strategies.

Artificial intelligence (AI) emerges as a transformative tool in medicine, offering potential improvements in diagnostics, prognostics, and personalized treatment planning (6,7). In CRC, AI has demonstrated promise in enhancing adenoma detection rates during colonoscopy, predicting outcomes from pathology slides, and tailoring therapies based on genomic data (8,9,10). Despite its rapid development, reflected in a peak in CRC-related AI publications in 2024 as described in *Fig. 1*, adoption remains limited due to high costs, regulatory barriers, and data infrastructure challenges.

This review critically examines the intersection of AI and CC care by evaluating the progress

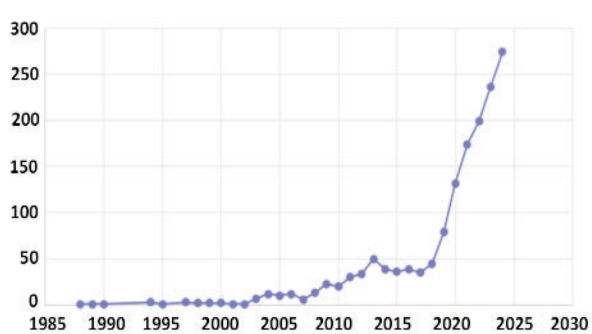

Figure 1. Annual number of scientific publications on colorectal cancer and artificial intelligence (1988–2024). The graph illustrates the growing research interest in the application of AI to colorectal cancer, with a marked increase in publication volume beginning around 2015 and reaching its peak in 2024. Data were retrieved from the PubMed database.

achieved to date, structured around key stages in the management of CC patients. *Fig. 2* illustrates the conceptual integration of artificial intelligence across key stages in the modern management of colon cancer and serves as a visual abstract of the review.

AI in Colon Cancer Diagnosis

AI in Colonoscopy and Polyp Detection

High-definition colonoscopy remains the primary modality for CRC prevention, yet conventional practice continues to miss a substantial proportion of adenomas (11-14). To address this diagnostic gap, deep learning-based computer-aided detection (CADe) systems have been introduced. These systems provide real-time visual alerts when mucosal patterns suggest the presence of polyps, thereby assisting endoscopists during procedures (11-14).

Multiple multicenter randomized controlled trials (RCTs) have consistently demonstrated that CADe enhances adenoma detection rate (ADR) by 25–50% (11-14). Recent evidence shows that AI-assisted colonoscopy markedly improves detection outcomes. Barua et al. (13) reported an ADR increase from 19.3% to 29.6% and a relative risk (RR) of 1.52 and a polyp detection rate (PDR) increase from 30.6% to 45.4% with RR of 1.48, with the greatest gains for diminutive adenomas. Similarly, Xu et al. (15) found higher ADR (39.9% vs 32.4%) and advanced ADR (6.6% vs 4.9%) with benefits across both expert and non-expert endoscopists (12,13). The greatest impact is observed in the detection of diminutive (≤5 mm) and small (6–9 mm) tubular adenomas, which are often implicated in interval cancers (11-14). In contrast, the detection of advanced adenomas (>10 mm or those with high-grade dysplasia) remains largely unchanged (12,15,16).

Recent studies have reinforced these findings, with an RCT demonstrating a near doubling of sessile serrated lesion (SSL) detection rates (4.7% vs. 2.0%; p = 0.01) without prolonging withdrawal time (17). In a large real-world U.S. cohort, combining CADe with a mucosal exposure device (EndoCuff™) yielded further improvements, raising right-sided SSL detection from 12.3% to

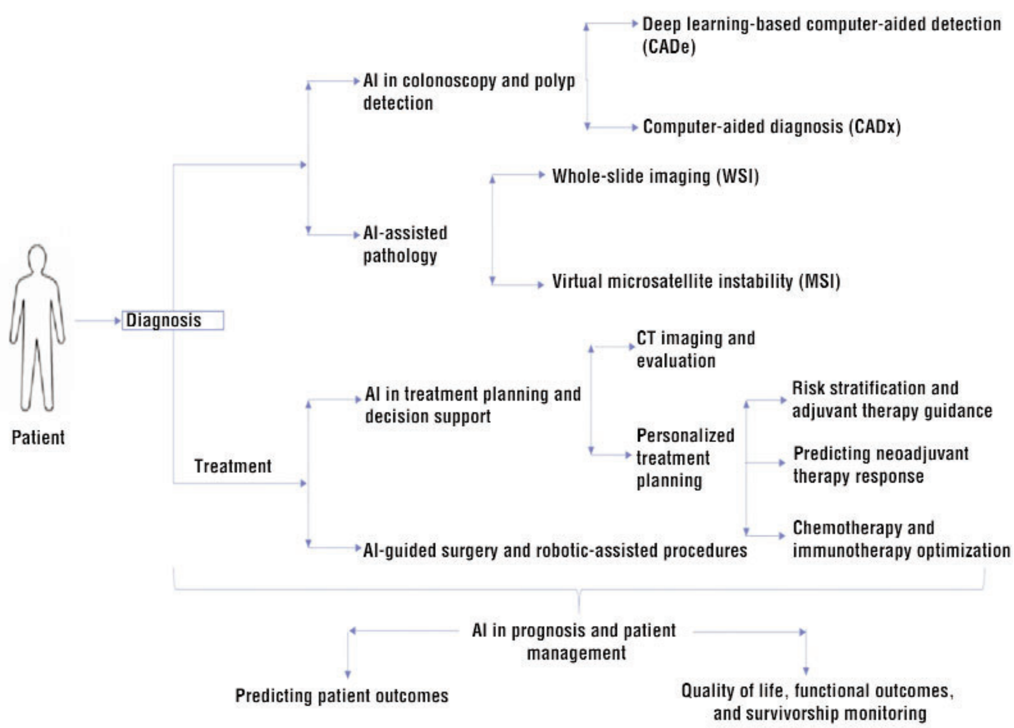

Figure 2. Visual abstract illustrating how artificial intelligence enhances colorectal cancer care – supporting diagnosis, guiding personalized treatments, assisting surgery, and monitoring patients to improve outcomes and quality of life.

24.8% and increasing overall SSL detection for 1–5 mm lesions from 9.6% to 17.1% (18). However, a seven-center international RCT highlighted inter-operator variability: while CADe increased SSL detection per colonoscopy by 58%, it offered limited benefit among endoscopists with high baseline detection rates (18).

Concerns that CADe may increase false-positive resections or significantly prolong procedure time remain unproven (11,14). Across pragmatic trials, non-neoplastic resection rates remained stable, and the median withdrawal time rose by less than one minute – an acceptable trade-off in clinical practice (11,14). No device-related adverse events have been reported to date (11,14). Nevertheless, professional societies emphasize that AI should act as a "second observer" rather than a replacement for rigorous inspection technique (11,14). Ongoing prospective registry studies aim to determine whether CADe-associated increases in ADR ultimately translate into lower rates of interval CRC (14).

Computer-aided diagnosis (CADx) represents the next stage in AI integration (19,20). These systems analyze image-enhanced endoscopic modalities, such as narrow-band imaging, blue light imaging, and i-scan, to classify lesions in situ as neoplastic or non-neoplastic (19,20). i-scan is a digital, dye-less image enhancement technology that modifies endoscopic images in real time through algorithm-based processing, by applying surface enhancement to emphasize mucosal borders, contrast enhancement to highlight subtle depressions, and tone enhancement (TE) to optimize vascular and mucosal patterns, i-scan improves visualization of colorectal lesions without the need for topical dyes (19,20). Recent systematic reviews and prospective studies have shown that i-scan, particularly in high-definition colonoscopy, increases the adenoma detection rate compared with white light endoscopy, with diagnostic accuracies frequently reported in the 80-90% range – values that approach expert optical diagnosis (19,20). However, despite these advantages, the negative predictive value for diminutive recto-sigmoid hyperplastic polyps remains suboptimal (19,20). Consequently, a "diagnose-and-leave" strategy for such lesions cannot yet be endorsed in routine clinical practice and should be confined to controlled research protocols (19,20).

To improve performance, ongoing algorithmic refinements focus on expanding training datasets to include more serrated lesions and incorporating both spatial and temporal imaging features to improve diagnostic stability during peristalsis (20-22). Several CADx platforms are currently undergoing regulatory review, and expert consensus statements have begun to acknowledge the potential utility of AI-assisted optical biopsy in reducing histopathology costs – provided that validated performance thresholds are met (20,21).

In summary, AI is rapidly transforming the landscape of CC endoscopy, with CADe systems already demonstrating clinically meaningful improvements in adenoma and serrated lesion detection. These advances hold promise for reducing interval cancers and improving patient outcomes, particularly when integrated into routine practice alongside high-quality inspection techniques. While early results for CADx are encouraging, further validation is needed to establish its role in real-time histological assessment and cost-effective management strategies. As regulatory frameworks evolve and clinical data mature, AI-assisted colonoscopy is poised to become a central component of precision medicine, offering enhanced diagnostic accuracy without compromising procedural safety or efficiency.

AI-Assisted Pathology

The integration of artificial intelligence (AI) into digital pathology is reforming (CRC) diagnostics, offering scalable, objective, and highly reproducible tools for histological analysis. Whole-slide imaging (WSI) technology enables the digitization of traditional glass slides into high-resolution, gigapixel images that are suitable for deep convolutional neural network (CNN) analysis (23). These advances have facilitated the development of AI-powered diagnostic tools capable of triaging pathology slides by automatically distinguishing normal from abnormal tissue and flagging regions suspicious for dysplasia with sub-millimeter accuracy (23).

In a large retrospective validation involving colorectal biopsy specimens from the UK and Portugal, the CAIMAN AI model achieved a sensitivity of 99% for detecting clinically significant large-bowel conditions, including colorectal carcinoma, high-grade dysplasia, and active inflammatory bowel disease (23). In parallel, the system demonstrated a specificity of 60% for identifying histologically normal mucosa, enabling automated clearance of over half of benign biopsies (23). These performance characteristics suggest a substantial potential to reduce histopathologist workload while maintaining a very low risk of false-negative diagnoses (23). Comparable AI systems applied to colectomy specimens can efficiently localize tumor foci, assess surgical resection margins, and quantify lymphovascular invasion (23). These applications not only improve turnaround time but also contribute to the standardization of pathology reporting, particularly in high-volume centers (23).

Beyond diagnostic triage, AI has shown growing potential *in silico* molecular profiling. Recent studies have demonstrated that histomorphological features embedded within routine hematoxylin and eosin (H&E) slides can predict microsatellite instability (MSI) with area under the curve (AUC) values between 0.82 and 0.90 (24). Such virtual MSI screening could serve as a cost-effective pre-screening tool, guiding confirmatory immunohistochemistry or PCR testing and accelerating the identification of Lynch syndrome and eligibility for immune checkpoint inhibitors (24). Prediction of hotspot mutations such as KRAS and BRAF is more complex due to the more subtle morphological cues; however, emerging deep learning models have reported promising AUCs around 0.75, with further gains anticipated as more ethnically diverse and well-annotated training datasets become available (24).

AI is also advancing risk stratification in CRC pathology. Deep learning algorithms can now quantify prognostic features such as tumor budding, immune cell infiltration, and stromal composition to construct multimodal digital biomarkers that serve as independent predictors of patient outcomes (9)."

In a pivotal validation study involving more than 4,000 digitized slides, a deep learning-derived prognostic index achieved a concordance score of 0.76 – surpassing traditional TNM staging – and reclassified nearly 25% of stage II patients into different risk categories, potentially altering recommendations for adjuvant chemotherapy (9). The concordance score, also referred to as the C-index, quantifies the discriminative ability of a prognostic model: values range from 0.5 (no better than chance) to 1.0 (perfect prediction), with higher scores indicating superior accuracy in correctly ranking patient survival times (9). Similarly, a multi-institutional model analyzing T1 CRC resection specimens achieved an AUC of 0.76 in predicting lymph node metastasis, thereby identifying patients at low metastatic risk who may safely avoid unnecessary colectomies without compromising oncological safety (25).

While these advances are promising, real-world implementation requires cautious and systematic integration. External validation across a variety of scanners, staining protocols, and patient populations is essential to ensure generalizability and performance consistency (19). Transparency and interpretability remain key challenges; many commercial platforms now include saliency maps and feature attribution tools to enhance user trust and facilitate clinical adoption (19). Saliency maps are visual overlays that highlight the image regions most influential in driving the prediction of the model, thereby allowing the endoscopist to understand why a polyp was flagged as suspicious (19). Feature attribution tools, on the other hand, quantify the relative contribution of specific variables or image characteristics to the final output, providing an additional layer of interpretability and ensuring that predictions are not perceived as "black-box" results (19). Regulatory bodies such as the Food and Drug Administration (FDA) and European Medicines Agency EMA have instituted guidelines requiring post-market surveillance to monitor algorithmic performance drift over time (19). Crucially, professional societies emphasize that AI tools are designed to augment – not replace – clinical decision-making, and that ultimate diagnostic responsibility remains with the pathologist (19).

CADe systems are already cost-effective in CRC screening, combining low implementation costs with savings from better detection and prevention, while cost models for AI-assisted digital pathology now factor in equipment, digitization, and labor efficiencies (19). As reimbursement frameworks evolve, demonstrating long-term clinical utility and economic sustainability will be essential to widespread adoption (19).

AI-enabled digital pathology represents a transformative shift in CC care, with the potential to enhance diagnostic accuracy, accelerate molecular profiling, and refine the predictions, ultimately improving clinical outcomes and resource allocation. While many algorithms have achieved promising performance in retrospective and multicenter validations, their integration into clinical workflows must be accompanied by rigorous validation, interpretability tools, and ongoing oversight to ensure equity, safety, and transparency. As digital infrastructure matures and regulatory frameworks adapt, AI-powered pathology is set to become a cornerstone of precision oncology in CC cancer, bridging the gap between high-throughput diagnostics and personalized patient care.

AI in Treatment Planning and Decision Support

AI in CT Imaging and Evaluation

Deep learning-based algorithms applied to contrast-enhanced CT scans performed without bowel preparation have demonstrated high diagnostic performance in colon cancer detection, with reported accuracy of 97.2%, sensitivity of 95.9%, and specificity of 98.3% in internal validation (26). External validation datasets further confirmed the consistency of these results, with area under the curve (AUC) values ranging from 0.957 to 0.994, exceeding the diagnostic performance of radiologists working unaided (26). In comparative analyses, radiologist accuracy increased from 86.0% to 93.4% when supported by AI, with similar gains observed across external datasets (from 85.3% to 93.6%, $p < 0.0001$) (26). Furthermore, the AI system detected additional cancer cases missed during standard reading, highlighting its potential to reduce oversight and enhance early detection (26).

Advances in deep learning-based segmentation, including Sharp U-Net – a modified U-Net architecture that uses sharpening filters and depth wise convolutions to enhance boundary detection – have improved the automated delineation of tumor margins and identification of regional lymph nodes on CT and MRI (27). By increasing spatial precision and minimizing segmentation artifacts, these models support more accurate and consistent TNM staging, with reported improvements of over 2% in segmentation metrics compared to baseline architectures (27).

Beyond anatomic visualization, AI enables radiomic analysis by first segmenting the region of interest, such as a tumor, on CT or MRI scans, followed by the extraction of quantitative features that describe the texture, shape, edge sharpness, intensity distribution, and spatial complexity of the lesion (28,29). These features are computed using mathematical filters and algorithms that quantify patterns within the image pixel matrix, capturing tumor heterogeneity and microenvironmental characteristics that are not discernible through visual inspection alone (28,29). These radiomic features have been leveraged to develop imaging biomarkers that provide insights into tumor biology, including aggressiveness, proliferation potential, and therapeutic response (28,29). Notably, several studies have demonstrated that radiomic signatures derived from CT scans can differentiate microsatellite instability-high tumors from microsatellite-stable subtypes with clinically meaningful accuracy, achieving AUC values of up to 0.894 in training cohorts and 0.839 in independent test sets (28,29). This distinction is critical, as MSI status informs both prognosis and eligibility for immunotherapy (28,29).

In parallel, machine learning-based texture analysis of contrast-enhanced CT images has shown promising performance in predicting key oncogenic mutations, such as KRAS, which influences responsiveness to epidermal growth factor receptor targeted therapies (30). This approach involves extracting quantitative radiomic features, such as texture uniformity, entropy, and edge sharpness, from segmented tumor regions, followed by classification using supervised algorithms like AdaBoost or support vector machines (30). In a retrospective study, a combined clinical-radiomic model achieved an accuracy of 76.8%, with sensitivity of 73.3% and specificity of 80.8% in identifying KRAS mutations (30). Compared to conventional tissue-based genotyping, which requires invasive sampling and may suffer from sampling bias or intra-tumoral heterogeneity, radiomic analysis enables a noninvasive, full-volume assessment that captures the spatial complexity of the entire tumor. These applications illustrate the emerging concept of a "virtual biopsy," where imaging phenotypes are computationally linked to molecular features, offering a scalable and patient-friendly alternative to tissue-based profiling (30).

The integration of AI into CT-based evaluation of colorectal cancer represents a major advance in diagnostic radiology and precision oncology (31,32). From improving lesion detection and staging accuracy to enabling non-invasive molecular profiling through radiomics, AI systems provide radiologists and oncologists with powerful tools for early, personalized, and data-driven decision-making (31,32). As these technologies continue to evolve, with increasingly sophisticated algorithms and larger, more diverse datasets, their clinical utility is expected to expand (31,32). Nonetheless, successful implementation will require careful validation, interpretability safeguards, and workflow integration to ensure reliability and clinician trust. Ultimately, AI-enhanced imaging is poised to become a cornerstone of individualized care in CRC management.

AI in Personalized Treatment Planning

The integration of artificial intelligence into personalized treatment planning for CC has become increasingly essential due to the growing complexity and heterogeneity of the disease (1,3,29). Standardized treatment guidelines, while foundational, often fail to accommodate the extensive inter-patient variability, intratumoral molecular diversity, and frequent coexistence of comorbid conditions that characterize modern oncological cases (1,3,29). AI provides the computational power necessary to synthesize high-dimensional data, including genomic, radiological, histopathological, and clinical parameters, into actionable insights (1,3,29). This facilitates refined prognostic stratification, prediction of therapy response, and dynamic adaptation of therapeutic strategies to each patient's unique profile, thereby surpassing the limitations of static treatment algorithms (1,3,29)

Risk stratification and adjuvant therapy guidance

One of the most challenging decisions in stage II colorectal cancer is whether to administer adjuvant chemotherapy (29,33). Although most patients have a favorable prognosis, a subset, such as those with microsatellite instability or adverse histologic features, are at higher risk of recurrence and may benefit from systemic therapy (29,33). However, clinical identification of these patients is often imprecise, making the decision particularly nuanced, as it requires balancing the risks of overtreatment and its toxicities against the danger of undertreatment and missed therapeutic opportunity (29,33). AI models assist treatment decisions by integrating clinical, molecular, and spatial data to improve recurrence risk prediction and personalize therapy in stage II colorectal cancer (29,33). Trained on histopathology and gene expression data, these algorithms stratify patients more accurately than conventional methods by detecting subtle features, such as tumor budding, immune infiltration, and stromal architecture, more effectively than the human eye, through objective, pixel-by-pixel analysis of whole-slide images (29,33). This precision reduces inter-observer variability and helps avoid unnecessary chemotherapy in low-risk patients (29,33).

Predicting neoadjuvant therapy response

In rectal cancer, a related but distinct subset of colorectal malignancies, neoadjuvant chemoradiotherapy is routinely indicated for patients with stage II (T3–T4, N0) and stage III (any T, N+) disease, this approach aims to reduce tumor volume, improve resectability, increase sphincter preservation rates, and lower the risk of local recurrence (34). By downstaging the tumor before surgery, neoadjuvant therapy contributes to better oncological and functional outcomes (34). AI applications in this context have focused on predicting pathological complete response (pCR), a surrogate marker of excellent prognosis and a potential gateway to non-operative management (34). When pCR is achieved – typically confirmed through clinical, radiological, and endoscopic assessment – some patients may be eligible for a "watch-and-wait" strategy, thereby avoiding surgery and its associated morbidity (34).

Radiomics and DL models analyzing baseline MRI or CT imaging, sometimes combined with clinical and laboratory data, have demonstrated strong predictive performance, with AUC values ranging from 0.80 to 0.90 in several studies (34). This predictive capability is clinically valuable because early identification of likely responders to neoadjuvant therapy can inform personalized treatment planning, guide decisions about intensification or de-escalation of therapy, and potentially support the selection of patients for non-operative management in the case of expected complete response (34).

These models enable clinicians to consider more conservative management for complete responders, potentially avoiding major surgery and its associated morbidity (e.g., bowel dysfunction, sexual dysfunction, or permanent stomas). Integration of such AI tools into pre-treatment planning pathways is expected to personalize rectal cancer therapy more effectively and improve patient quality of life.

Therapeutic target identification through multi-omics AI

Beyond clinical risk prediction, AI is driving hypothesis-generating research in therapeutic development through multi-omics integration. Deep learning models capable of analyzing genomic, transcriptomic, proteomic, and immunological data can identify novel oncogenic pathways and potential drug targets (35). A recent study, for instance, used a deep learning framework to uncover a macrophage-related gene module associated with immune suppression and disease progression in CRC, offering potential avenues for immunotherapy modulation (35).

Such integrative analyses are computationally intensive and typically beyond the scope of conventional statistical approaches. AI enables the detection of non-linear and higher-order interactions between biological variables, accelerating the discovery of personalized treatment targets and biomarkers.

AI in chemotherapy and immunotherapy optimization

AI is also being applied to personalize systemic therapy regimens, including both cytotoxic chemotherapy and immunotherapy (29). Machine learning models trained on clinical trial data and electronic health records (EHRs) are being developed to recommend optimal drug combinations and dosing schedules tailored to individual patient profiles (29). These models incorporate tumor genomics, prior treatment responses, comorbidities, and even pharmacogenomic data to predict efficacy and toxicity (29).

In the realm of immunotherapy, predicting response remains a significant challenge. AI models incorporating radiomic features, mutational burden, microsatellite instability status, and immune cell infiltration patterns are being actively developed to predict patient responses to immune checkpoint inhibitors (34). Radiomics enables the extraction of high-dimensional features from imaging modalities such as CT or MRI, capturing intratumoral heterogeneity that is often invisible to the human eye (34). When combined with genomic markers, including tumor mutational burden and MSI status, these models can provide a more nuanced representation of tumor biology (34). Furthermore, integration of immune-related variables, such as the density and spatial distribution of tumor-infiltrating lymphocytes, enhances the capacity to assess the functional status of the tumor microenvironment (34). Collectively, such multimodal frameworks offer a holistic view that may surpass the predictive value of conventional single biomarkers, including PD-L1 expression or tumor mutational burden alone, thereby improving patient stratification and guiding precision immunotherapy in colon cancer (34).

Artificial intelligence is rapidly transforming personalized treatment planning by integrating vast and complex datasets across diagnostic domains, AI models enable nuanced risk assessment, individualized therapy selection, and data-driven clinical decision-making (34). Applications range from predicting adjuvant chemotherapy benefit and neoadjuvant response to identifying new immunological targets and tailoring systemic therapies based on genomic and imaging profiles (34).

While the translational promise of AI is clear, significant work remains to bring these tools into everyday clinical use. Key challenges include the need for large, diverse, and well-annotated training datasets; external validation across multiple populations and institutions; explainability of AI outputs; and seamless integration into clinical workflows. Nevertheless, as these challenges are addressed through multidisciplinary collaboration, AI is poised to become an integral component of precision oncology, improving survival and quality of life for patients with colon cancer (29,33-35).

AI-Guided Surgery and Robotic-Assisted Procedures

Surgical management of CC is undergoing a paradigm shift through the integration of artificial intelligence (AI), augmented intelligence, and advanced robotic platforms (36). Robotic-assisted surgery, led by systems such as the da Vinci Surgical System, has become increasingly adopted for colorectal procedures due to its enhanced dexterity, three-dimensional visualization, and ergonomic precision (36). Comparative studies suggest that robotic colectomy may offer clinical advantages over conventional laparoscopy, including reduced postoperative pain, shorter hospital stays, and improved surgical quality – evidenced by higher lymph node yields and lower rates of postoperative ileus (36).

Beyond the mechanical capabilities of robotic systems, AI is increasingly being embedded into the surgical workflow to support intraoperative decision-making (37). One of the most promising advancements in this domain is the development of AI-powered computer vision systems for real-time anatomical recognition (37). These technologies leverage deep learning to analyze laparoscopic video streams and highlight critical structures such as vasculature and pelvic nerves, thereby improving intraoperative safety and enhancing the training experience (37).

Notably, the experimental "Eureka" system demonstrated high accuracy in identifying pelvic nerves during colorectal resections, reducing the risk of iatrogenic injury, especially among surgical trainees (37). In a study involving 101 laparoscopic colorectal procedures, the AI-assisted system correctly identified the right lumbar splanchnic nerves in 90.6% and the left lumbar splanchnic nerves in 88.6% of cases where trainees initially failed to do so (37). This assistance significantly enhanced anatomical recognition in high-risk zones, potentially improving surgical safety and offering a powerful educational tool, especially for less experienced operators (37).

Another emerging application involves the interpretation of intraoperative fluorescence imaging, such as indocyanine green (ICG) angiography (38). AI algorithms trained to evaluate perfusion dynamics can classify intestinal segments based on vascular adequacy, thereby guiding anastomotic site selection and potentially reducing the incidence of anastomotic leaks (38). These systems offer real-time perfusion assessment that surpasses subjective visual evaluation, promoting safer and more standardized surgical decision-making (38).

AI is also advancing the automation and augmentation of surgical processes through phase recognition and instrument tracking (38). Using annotated operative videos, machine learning models can now recognize different phases of colorectal surgery and detect surgical instruments in real time (38). These capabilities lay the groundwork for intraoperative applications such as automated camera control, workflow optimization, and real-time prompts for critical procedural steps (38). In addition, AI models developed by Celotto et al. in 2024 integrate intraoperative and clinical variables, such as tumor location, operative time, intraoperative blood loss, neoadjuvant therapy, ASA score, and preoperative albumin, to predict complications like anastomotic leakage (3%–21% incidence), surgical site infections, and bleeding. Some models achieved an AUROC of 0.86 for predicting postoperative bleeding by day two, demonstrating strong potential for perioperative risk assessment (38). Such predictive analytics can support risk-adapted intraoperative strategies, including the selective use of protective stomas for high-risk patients (38).

A comprehensive overview of the principal applications of artificial intelligence in colon cancer - including the AI techniques employed, data sources analyzed, and reported clinical impact across diagnostic, therapeutic, prognostic, and survivorship domains - is provided in *Table 1*.

Although fully autonomous surgery remains a long-term aspiration, the convergence of AI with robotic systems is already delivering measurable clinical benefits. Current implementations demonstrate that AI-guided, robot-assisted surgery can enhance precision, consistency, and patient safety. Importantly, these technologies are not intended to replace the surgeon, but to augment clinical decision-making and support procedural excellence. Ongoing research and validation studies continue to refine these capabilities, pointing toward a future in which increasingly intelligent surgical systems play a central role in colon cancer care (38).

AI in Prognosis and Patient Management

AI for Predicting Patient Outcomes

AI-based models have demonstrated superior prognostic performance compared to conventional staging systems such as TNM (31). For example, a recent study validated a deep learning algorithm trained on routine hematoxylin and eosin (H&E)-stained slides that identified high-risk stage III colon cancer patients with a nearly nine-fold increased hazard of recurrence (31). This model allowed for clear discrimination between low- and high-risk cohorts, offering refined survival predictions beyond traditional parameters (31,39,40).

Kos et al. demonstrated that multiple machine learning models, including decision trees, ensemble

Table 1. Summarizes key applications of artificial intelligence in colon cancer across multiple domains, including endoscopy, pathology, imaging, prognosis, surgery, and quality of life prediction. For each area, it outlines the AI techniques used, the types of data analyzed, and the main clinical outcomes reported between 2020 and September 2025.

AI Application Domain	AI Technique	Data Type	Clinical Impact	Key References
Colonoscopy & polyp detection	CNN, real-time CADe	Colonoscopy video	↑ Adenoma detection rate (ADR) (25–50%), ↓ interval cancers	(37–41), (50–51)
Digital pathology	CNN, deep learning	Whole-slide images (WSI)	Automated grading, MSI prediction, molecular profiling	(46–47), (9), (48)
CT imaging & radiomics	CNN, radiomics, texture analysis	CT, MRI	Tumor margin delineation, KRAS/MSI prediction, staging accuracy	(14–18)
Prognosis & recurrence prediction	Gradient Boosting, XGBoost, CNN	Clinical data + WSSI + CT/MRI	Risk stratification, survival prediction, therapy guidance	(25–31)
AI-guided surgery	Computer vision, deep learning	Intraoperative video, ICG fluorescence	Nerve recognition, perfusion assessment, surgical precision	(22–24)
Quality of life (QoL) prediction	Multimodal machine learning	Clinical, imaging, patient-reported outcomes (PROs)	Predicting QoL and functional recovery, personalized rehab	(32–33)

methods, and support vector machines, can predict long-term overall survival in non-metastatic colorectal cancer patients with high accuracy, achieving AUC values ranging from 0.84 to 0.92 across 1- to 10-year intervals (32). Similarly, supervised machine learning techniques, including gradient boosting and random forest classifiers, have been used to estimate 1-, 3-, and 5-year survival in non-metastatic colorectal cancer patients with strong predictive performance (41), In a retrospective study conducted by Liu et al., the XGBoost model demonstrated excellent accuracy in predicting long-term outcomes, achieving an AUC of 0.962 in training, 0.952 in internal validation, and 0.91 in external validation, based solely on 44 clinical, pathological, and intraoperative variables as shown in *Table 2* (41).

AI-driven analysis of digitized histopathology slides has uncovered morphological features predictive of recurrence (42). Specifically, the study by Kim et al. applied a deep learning-based platform (Lunit SCOPE IO) to automatically quantify tumor-stroma ratio (TSR) and cancer-associated fibroblast (CAF) density from whole-slide images in a cohort of 207 stage II and III colorectal cancer patients (42,43). Deep learning frameworks combining CNN-based tissue segmentation and supervised classification algorithms stratified patients into prognostic subgroups (42). Both low TSR and high CAF density were identified as independent predictors of shorter disease-free survival (log-rank $p<0.0001$ and $p=0.017$, respectively) (42). When integrated with traditional high-risk clinicopathological features, these AI-derived biomarkers improved recurrence risk classification and reduced false-negative rates (42). These findings demonstrate the ability of the model to extract prognostically relevant microenvironmental features, such as stromal quality and fibroblast abundance, which are often imperceptible to human observers (42).

AI-based tools have also enabled detailed evaluation of the tumor microenvironment (43). For instance, deep learning-powered quantification of tumor-stroma ratio and fibroblast density has significantly enhanced the stratification of disease-free survival in stage II–III colorectal cancer patients (43). In addition to histopathological analysis, AI has been employed to model post-surgical outcomes by integrating clinical data with imaging features extracted from CT scans (43). Rhanoui et al. introduced a multimodal machine learning framework that combines clinical indicators and radiological data through a specialized module called the Quality of the Microenvironment eNcoding Unit (QMNU), which learns relevant representations of the tumor microenvironment directly from medical imaging (43). This approach enabled the prediction of key quality-of-life scores such as Wexner and AUR, achieving up to 96% accuracy for AUR when both modalities were combined (43).

Table 2. Summarizes the 44 clinical, pathological, and perioperative variables used to train the XGBoost model for predicting colon cancer recurrence.

Category	Variables
Demographic & Lifestyle	Gender, Age, Smoking history, Alcohol history, Body Mass Index (BMI)
Preoperative Clinical Data	ASA score, NRS-2002 (nutritional risk score), Surgical history, Disease duration, Adjuvant chemotherapy history, Adjuvant radiotherapy history
Comorbidities	Anemia, Diabetes, Ileus, Hypertension, Hyperlipidemia, Coronary artery disease
Preoperative Lab Markers	Albumin, CEA, CA19-9, CA125, CA72-4
Tumor Characteristics	T stage, N stage, Peripheral nerve invasion, Vascular invasion, Tumor size, Tumor number, Tumor configuration, Pathological type
Intraoperative Variables	Surgical approach, Type of surgery, Duration of surgery, Intraoperative bleeding, Number of lymph nodes retrieved, Emergency surgery status
Postoperative Variables	Postoperative CEA, CA19-9, CA125, CA72-4, Procalcitonin, C-reactive protein (CRP), Serum amyloid A (SAA), Neutrophil-to-lymphocyte ratio (NLR)
Outcome Variable	Tumor recurrence

By transforming subjective histopathological and functional assessments into objective, high-dimensional representations, AI has facilitated the identification of high-risk patients who would not have been recognized using conventional assessment methods (43). These models highlight the predictive value of the tumor microenvironment, not just in recurrence, but also in long-term patient well-being, and demonstrate the growing role of multimodal AI in personalizing care across the cancer trajectory (43).

The application of artificial intelligence in colon cancer prognosis and recurrence prediction represents a major advancement in precision oncology (39-43). From integrating clinical and imaging data to analyzing histological slides and the tumor microenvironment, AI-driven models provide robust, individualized estimates of recurrence and survival risk (39-43). These tools offer clinicians a more nuanced understanding of patient outcome and may guide decisions regarding adjuvant therapy intensity and surveillance strategies (39-43). As validation efforts continue and these models are embedded into clinical decision-support systems, AI is set to enhance the accuracy and personalization of post-treatment management in colon cancer (39-43).

Quality of Life, Functional Outcomes, and Survivorship Monitoring

In colon cancer, prognostic assessment increasingly extends beyond recurrence and survival, encompassing patient-centered outcomes such as post-treatment quality of life (QoL) and functional recovery (44). Artificial intelligence (AI) has demonstrated the ability to integrate heterogeneous data, including clinical characteristics, treatment variables, imaging features, and patient-reported outcomes (PROMs), to predict recovery trajectories (44). Early identification of patients at risk for persistent dysfunction, fatigue, or psychological distress enables timely referral to supportive interventions such as rehabilitation, nutritional support, or psycho-oncology, thereby personalizing survivorship planning (44,45).

Beyond prognostication, AI facilitates continuous survivorship monitoring. Natural language processing and machine learning applied to PROMs, electronic symptom diaries, and online forums allow the extraction of meaningful trends and patient concerns, generating dynamic "patient journey maps" that highlight difficulties with daily functioning, follow-up, or emotional well-being (45). In clinical practice, electronic PRO (ePRO) systems integrated with AI can detect subtle or cumulative symptom patterns, such as escalating pain, gastrointestinal disturbances, or fatigue, prompting earlier imaging or laboratory evaluation than scheduled surveillance would allow (45,46). Moreover, longitudinal analysis of PROMs supports the early recognition of functional or psychological distress and timely referral to supportive care services (46).

Although still in early stages, AI-based prediction of QoL and monitoring of survivorship outcomes represent a paradigm shift toward holistic and patient-centric cancer care, where functional outcomes and life quality are considered as integral to treatment success as recurrence or survival (44-46).

Challenges and Ethical Considerations

Despite promising advancements, the integration of AI into colon cancer care presents several technical, ethical, and regulatory challenges (47). Data privacy and security remain foundational concerns, as AI systems depend on large volumes of sensitive health information, including genomic, imaging, and clinical records (47). Ensuring compliance with regulations such as the General Data Protection Regulation (GDPR) and the Health Insurance Portability and Accountability Act (HIPAA) requires secure data pipelines, rigorous de-identification protocols, and robust cybersecurity infrastructure to prevent breaches and misuse (47).

Another major limitation involves algorithmic bias and equality (48). Many AI models are trained on datasets derived from single institutions or demographically homogeneous populations, which can limit their generalizability (48). This raises concerns about inequitable performance in under-represented groups, potentially exacerbating disparities in CC outcomes (48). For example, a model trained predominantly on data from high-income countries may underperform in low-resource settings, where the disease burden is rapidly increasing (48,49) In addition, most deep learning models currently operate as "black boxes," offering minimal transparency in how predictions are generated (48,49). This lack of interpretability impairs clinical trust, complicates regulatory evaluation, and limits adoption in high-stakes environments like oncology (49).

Regulatory and implementation barriers further complicate clinical integration (50). Existing medical device regulations are not fully equipped to address the dynamic, data-driven nature of AI tools, which can evolve over time through continuous learning (50). Regulatory bodies such as the FDA and EMA now require prospective clinical validation and post-market surveillance of AI-enabled platforms, but standardized benchmarks and performance thresholds remain under development (50). Additionally, integrating AI into existing clinical workflows demands infrastructure investment, interoperability with electronic health records, and clinician training, all of which may be difficult to scale – particularly in resource-constrained health systems (51).

Future Directions

Looking forward, several emerging trends are shaping the next frontier of AI in CC. Among the most promising is multimodal AI, which combines pathology, radiology, genomics, clinical variables, and patient-reported outcomes to deliver highly personalized predictions for diagnosis, prognosis, and therapy selection (50). Such approaches reflect the growing shift toward holistic precision oncology (50). Advances in federated learning – where models are trained across decentralized datasets without direct data sharing – may also help mitigate privacy risks and enable collaboration across international centers (52,53).

Nonetheless, substantial research gaps and implementation challenges remain, future studies must prioritize external validation across diverse populations, robust model explainability, and prospective evaluation of clinical impact (48,54,55). The development of transparent, ethically grounded frameworks for AI deployment is equally critical to ensure that these technologies enhance – rather than undermine – equity, autonomy, and trust in healthcare delivery (48,54,55).

Conclusion

Artificial intelligence is reshaping colon cancer management by improving accuracy, efficiency, and personalization at every stage – from detection to survivorship. AI-driven tools have shown clinical utility in enhancing adenoma detection during colonoscopy, supporting earlier diagnosis and reducing interval cancers. In pathology, deep learning applied to digital slides has improved diagnostic precision and enabled virtual biomarkers such as in silico MSI prediction, streamlining molecular testing and informing immunotherapy decisions.

AI also plays a key role in personalized treatment planning. By integrating clinical, imaging, and genomic data, machine learning models improve risk stratification and guide therapeutic decisions, including identifying stage II and III patients who may benefit from adjuvant chemotherapy. In surgical oncology, AI supports robotic systems by enhancing real-time anatomical recognition, perfusion assessment, and complication risk modeling, contributing to safer and more consistent colon resections.

Beyond survival outcomes, AI contributes to predicting quality-of-life and functional recovery, enabling a more holistic, patient-centered approach. Through analysis of patient-reported outcomes and symptom data, clinicians can detect early signs of clinical decline or psychological distress and intervene promptly.

While challenges remain, such as regulatory standards, data harmonization, and clinical adoption, AI is clearly evolving from experimental use to practical application. With continued validation and thoughtful integration, it is poised to become a core element of precision oncology in colon cancer.

Author's Contributions

OAB, CEM, CV conception and design of the study; OAB, CEM, FA, CA, IAB data acquisition; AT, TM, SOD analysis and interpretation of data, OAB, CEM, AC, CA, VH, IAB manuscript preparation, VH, CV, CEM, OAB manuscript editing, CV revising manuscript critically for important intellectual content. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

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Declaration of Generative AI and AI-assisted Technologies in the Writing Process

During the preparation of this work the author(s) used OpenAI. (2025, February 25). ChatGPT (Version 4) (Large language model). OpenAI. https://openai.com in order to improve the language and readability. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

Standard Data Availability Statement

This article is a narrative review and does not involve the generation or analysis of new datasets. All data referenced in this review are derived from previously published studies, which are cited within the manuscript. No additional datasets are available.

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