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DIAGNOSIS AND SCREENING OF COLORECTAL CANCER IN THE ELDERLY

DIAGNÓSTICO E RASTREIO DO CÂNCER COLORRETAL NO IDOSO

DIAGNÓSTICO Y CRIBADO DEL CÁNCER COLORRECTAL EN EL ADULTO MAYOR

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ABSTRACT

Colorectal cancer (CRC) is the third most common malignancy and the second leading cause of cancer-related death worldwide, with older adults representing the main risk group and the primary focus of early diagnosis and screening strategies. Traditional screening, based on colonoscopy and fecal tests, faces challenges related to adherence and invasiveness, driving the search for precision medicine approaches. Recent advances highlight the integration of biomarkers (proteomic and metabolic, such as oleic acid and allocoholic acid) and polygenic risk scores for individualized stratification and optimization of the ideal screening age. Artificial intelligence (AI) has also emerged as a powerful tool, using computed tomography classifiers to stratify recurrence risk in stage II CRC. Furthermore, molecular testing for KRAS and BRAF mutations is mandatory in advanced disease to guide more effective and less toxic targeted therapies. Circulating tumor DNA (ctDNA) stands out as a crucial non-invasive biomarker for detecting minimal residual disease and predicting recurrence, enabling individualized management. It is concluded that the future of CRC screening and diagnosis in the elderly lies in the convergence of liquid biomarkers, genomics, and AI, aiming at detection in curable stages and high-precision treatment.

Keywords: Colorectal Cancer. Screening. Elderly. Biomarkers. Precision Medicine.

RESUMO

O câncer colorretal (CCR) é a terceira neoplasia mais comum e a segunda principal causa de morte por câncer globalmente, sendo o idoso o principal grupo de risco e foco das estratégias de diagnóstico e rastreamento precoce. O rastreio tradicional, baseado em colonoscopia e testes fecais, enfrenta desafios de adesão e invasividade, impulsionando a busca por abordagens de medicina de precisão. Os avanços recentes destacam a integração de biomarcadores (proteômicos e metabólicos, como ácido oleico e alocólico) e escores de risco poligênico para estratificação individualizada e otimização

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da idade ideal de rastreio. A inteligência artificial (IA) também emergiu como uma ferramenta poderosa, utilizando classificadores de tomografia computadorizada para estratificar o risco de recorrência em CCR estágio II. Além disso, o diagnóstico molecular para mutações KRAS e BRAF é mandatório em doença avançada para guiar terapias-alvo mais eficazes e menos tóxicas. O DNA tumoral circulante (ctDNA) se destaca como um biomarcador não invasivo crucial na detecção de doença residual mínima e na predição de recidiva, permitindo o manejo individualizado. Conclui-se que o futuro do rastreio e diagnóstico do CCR no idoso reside na convergência de biomarcadores líquidos, genômica e IA, visando a detecção em estágios curáveis e o tratamento de alta precisão.

Palavras-chave: Câncer Colorretal. Rastreio. Idoso. Biomarcadores. Medicina de Precisão.

RESUMEN

El cáncer colorrectal (CCR) es la tercera neoplasia más frecuente y la segunda causa principal de muerte por cáncer a nivel mundial, siendo los adultos mayores el principal grupo de riesgo y el foco de las estrategias de diagnóstico y cribado precoz. El cribado tradicional, basado en colonoscopia y pruebas fecales, enfrenta desafíos de adherencia e invasividad, impulsando la búsqueda de enfoques de medicina de precisión. Los avances recientes destacan la integración de biomarcadores (proteómicos y metabólicos, como el ácido oleico y el ácido alocólico) y los puntajes de riesgo poligénico para la estratificación individualizada y la optimización de la edad ideal de cribado. La inteligencia artificial (IA) también ha surgido como una herramienta poderosa, utilizando clasificadores de tomografía computarizada para estratificar el riesgo de recurrencia en el CCR en estadio II. Además, el diagnóstico molecular de mutaciones KRAS y BRAF es obligatorio en la enfermedad avanzada para guiar terapias dirigidas más eficaces y menos tóxicas. El ADN tumoral circulante (ctDNA) se destaca como un biomarcador no invasivo crucial en la detección de enfermedad residual mínima y en la predicción de recurrencia, permitiendo un manejo individualizado. Se concluye que el futuro del cribado y diagnóstico del CCR en el adulto mayor reside en la convergencia de biomarcadores líquidos, genómica e inteligencia artificial, con el objetivo de detectar la enfermedad en estadios curables y proporcionar tratamientos de alta precisión.

Palabras clave: Cáncer Colorrectal. Cribado. Adulto mayor. Biomarcadores. Medicina de Precisión.

1 INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignant neoplasms globally, occupying a prominent position in both prevalence and mortality, especially in aging populations. It is the third most common neoplasm and the second leading cause of cancer death in the world, with a growing impact associated with increased life expectancy and demographic transition (Jing Sun et al., 2024; Huang et al., 2025). In this context, the elderly represent the main risk group, and are also the central focus of screening and early diagnosis strategies.

Colorectal carcinogenesis classically occurs through the adenoma-carcinoma sequence, characterized by progressive genetic, epigenetic, and metabolic alterations that transform the normal mucosa into premalignant lesions and, later, into invasive carcinoma. This multi-stage process offers an important window of opportunity for preventive interventions and effective screening, enabling the detection and removal of precursor lesions before progression to advanced stages (Yang Sun et al., 2024).

CRC screening has traditionally been based on methods such as colonoscopy and fecal testing, including fecal immunochemical testing (FIT), which are widely used for their effectiveness in reducing mortality. However, limitations such as the invasive nature of colonoscopy, high costs, and low population adherence have driven the development of alternative, less invasive, and more affordable approaches (Jing Sun et al., 2024). In this scenario, blood, metabolic, and proteomic biomarkers have emerged as promising tools for screening and early diagnosis.

Recent advances in precision medicine have allowed the incorporation of individualized risk models, which integrate clinical, genetic and molecular data. The use of polygenic risk scores, proteomic profiles, and circulating metabolites demonstrates potential to improve risk stratification and more accurately define the ideal age to start screening, especially in elderly and more vulnerable populations (Jing Sun et al., 2024). In addition, systemic metabolic changes associated with RCC, identified in plasma and feces, reinforce the role of biomarkers in early detection and understanding of tumor biology (Yang Sun et al., 2024).

At the same time, the molecular characterization of CRC has assumed a central role in diagnosis and therapeutic management, especially in advanced stages. Mutations in genes such as KRAS and BRAF are associated with distinct tumor subtypes, with a relevant prognostic and therapeutic impact, in addition to influencing the response to

targeted therapies and chemotherapy (Yaeger et al., 2024; Elez et al., 2025). These advances reinforce the need for integration between screening, early diagnosis, and personalized medicine.

Thus, the diagnosis and screening of colorectal cancer in the elderly represent a field in constant evolution, in which the combination of traditional methods with new diagnostic technologies and individualized predictive models can contribute significantly to the reduction of morbidity and mortality and to the optimization of public health strategies.

2 METHODOLOGY

The present study is characterized as a narrative literature review, developed with the objective of synthesizing and analyzing the most recent scientific evidence related to the diagnosis and screening of colorectal cancer in the elderly population. Data mining was performed in the PubMed database, using the descriptors "Colorectal Cancer" and "Elderly", articulated according to the terminology of the Medical Subject Headings (MeSH). Articles published in the last five years (2020-2025), available in full and written in English or Portuguese, that addressed biomarkers, advanced imaging techniques, and risk stratification were included. Studies focused exclusively on palliative care or animal models with no direct human clinical correlation were excluded. The selection involved screening of titles and abstracts, followed by the evaluation of full texts to confirm diagnostic relevance. The information extracted was organized in a descriptive way.

3 RESULTS

Recent literature highlights significant advances in the use of "omics" for early diagnosis. Integrated plasma and fecal metabolomics allowed the identification of specific metabolic signatures of adenoma-carcinoma progression. Oleic acid has been identified as enriched in RCC, while allocholic acid is depleted, serving as potential high-sensitivity diagnostic biomarkers (Yang Sun et al., 2024). In addition, plasma proteomics, when integrated with polygenic risk scores (PRS) and non-genetic factors (QCancer-15), demonstrated superior ability to predict the onset of CRC, allowing the personalization of the initial screening age (Jing Sun et al., 2024).

In the field of digital imaging and pathology, the use of artificial intelligence (AI) has emerged as a powerful tool. A deep learning-based computed tomography (CT) classifier

has been validated to stratify risk in patients with stage II RCC. This technology aids in the identification of patients at high risk of recurrence who would benefit from adjuvant chemotherapy, surpassing the accuracy of conventional pathological markers alone (Huang et al., 2025).

For the diagnosis of advanced or metastatic disease, which frequently affects the elderly population with multiple comorbidities, molecular diagnosis is mandatory. Studies such as BREAKWATER and KRYSTAL-1 reinforce the need for testing for BRAF V600E and KRAS G12C mutations at initial diagnosis. The combination of targeted therapies, such as encorafenib and cetuximab, demonstrated significantly higher response rates than conventional chemotherapy in patients with BRAF mutation, transforming the prognosis of this subpopulation (Kopetz et al., 2025; Elez et al., 2025). Similarly, the use of adagrasib plus cetuximab in cases of KRAS G12C mutation offers an effective and safe alternative for the management of previously treated patients (Yaeger et al., 2024).

In addition, the incorporation of these technologies has a direct impact on risk stratification and therapeutic decision-making. The role of circulating tumor DNA (ctDNA) as a non-invasive biomarker in the detection of minimal residual disease and in the prediction of recurrence is highlighted, allowing the identification of patients at higher risk after curative treatment. Recent evidence demonstrates its usefulness in selecting patients for adjuvant therapy, contributing to a more individualized approach and avoiding unnecessary treatments (TIE et al., 2022; NAKAMURA et al., 2024; REINERT et al., 2025; MARTÍNEZ-CASTEDO et al., 2025).

4 DISCUSSION

The discussion about CRC screening in the elderly reflects the shift from the "one size fits all" paradigm to "precision medicine". The integration of biomarkers discussed by Jing Sun et al. (2024) suggests that screening can be anticipated or postponed based on individual proteomic and genetic profile, optimizing health system resources. The challenge in implementing these new tools lies in laboratory standardization and cost-effectiveness compared to traditional FIT. In this context, the growing role of circulating tumor DNA (ctDNA) is also highlighted, whose application has demonstrated high sensitivity in detecting minimal residual disease and predicting recurrence, allowing for more individualized screening and follow-up strategies (TIE et al., 2022; NAKAMURA et al., 2024; MARTÍNEZ-CASTEDO et al., 2025).

The role of artificial intelligence in CT image analysis (Huang et al., 2025) represents a qualitative leap in diagnosis, allowing routine diagnostic imaging to provide deep prognostic data without additional invasive procedures. This is particularly relevant for the elderly, for whom the reduction of unnecessary invasive interventions is a priority. Additionally, prognostic models such as IRIS-CRC have demonstrated superior risk stratification capacity by integrating clinical and molecular variables, contributing to more accurate decisions regarding the need for adjuvant treatment (HUANG et al., 2023).

Finally, the mandatory molecular testing (KRAS/BRAF) in the diagnosis of metastases underlines that CRC should no longer be treated as a single disease (Ahn et al., 2024; Elez et al., 2025). The ability to predict resistance to certain chemotherapies through mutational profiling allows the clinician to select less toxic and more effective regimens while preserving the quality of life of the elderly patient (Yaeger et al., 2024). It is concluded that the future of CRC diagnosis and screening lies in the convergence between liquid biomarkers, genomic analysis and AI support, aiming at detection in curable stages and high-precision personalized treatment.

5 CONCLUSION

The screening and diagnosis of Colorectal Cancer (CRC) in the elderly population, which represents the main risk group, are undergoing profound transformation, evolving from the paradigm of "one size fits all" to **precision medicine**. This revision epitomized the emergence of a highly individualized approach, based on the convergence of several advanced technologies. Risk stratification is being enhanced by the integration of proteomic and metabolic **biomarkers**, along with polygenic risk scores, which allows personalizing the optimal age of screening initiation and optimizing healthcare resources.

In disease management, **circulating tumor DNA (ctDNA)** has established itself as a non-invasive biomarker of crucial importance, providing high sensitivity in detecting minimal residual disease and predicting recurrence. Its application is vital to guide the decision of adjuvant therapy, enabling individualized management and reducing toxicity in elderly patients at low risk of recurrence. At the same time, **Artificial Intelligence (AI),** through computed tomography classifiers, offers a qualitative leap by providing deep prognostic data from routine images, helping in risk stratification (e.g., IRIS-CRC). Finally, molecular testing for KRAS and BRAF V600E mutations has become mandatory in the scenario of advanced disease, ensuring the selection of more effective and less toxic

targeted therapies, preserving the quality of life of the elderly patient. It is concluded that the future of combating CRC in the elderly lies in the full adoption of these genomic, liquid biopsy and AI tools, with the ultimate goal of maximizing detection in curable stages and providing the most accurate and least invasive treatment possible.

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