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ROLE OF ANGIOGENESIS AND MICROVASCULAR DENSITY IN TUMOR PROGRESSION OF COLORECTAL CANCER

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Relevance

Colorectal cancer remains a major cause of cancer-related morbidity and mortality globally. Although advances in surgical techniques and chemotherapy have improved survival rates, disease recurrence and metastasis remain common. Angiogenesis is essential for tumor expansion beyond 2–3 mm in diameter, providing oxygen and nutrients while facilitating tumor cell dissemination. The assessment of MVD and angiogenic factors such as vascular endothelial growth factor (VEGF) and CD34 expression has therefore become an integral part of cancer biology and prognostic evaluation. Angiogenesis, the formation of new blood vessels from pre-existing vasculature, is a fundamental biological process driving tumor growth, metastasis, and therapy resistance in colorectal cancer (CRC). Microvascular density (MVD), a quantitative measure of angiogenic activity, has emerged as a critical prognostic biomarker reflecting tumor aggressiveness and metastatic potential. This extended abstract discusses the pathophysiological mechanisms of angiogenesis in CRC, the clinical significance of MVD and related molecular markers, and their potential implications for targeted anti-angiogenic therapies.

Keywords:colorectal cancer; angiogenesis; microvascular density; VEGF; CD34; prognosis; biomarkers; tumor progression

Objective

To evaluate the prognostic and clinical significance of angiogenesis and microvascular density in colorectal cancer, with a focus on immunohistochemical and molecular biomarkers that regulate neovascularization and influence tumor progression.

Materials and Methods

The analysis was based on recent publications between 2018 and 2024, selected from PubMed, Scopus, and Web of Science databases. Search terms included 'colorectal cancer', 'angiogenesis', 'microvascular density', 'VEGF', 'CD34', and 'prognosis'. Eligible studies were those that investigated the association between MVD or angiogenic factors and clinical outcomes, including tumor stage, recurrence, and overall survival. Immunohistochemical quantification of MVD using endothelial markers such as CD31, CD34, and CD105 was emphasized, along with molecular analysis of VEGF and hypoxia-inducible factors.

Results

High MVD correlates with advanced tumor stage, lymphovascular invasion, and distant metastasis in colorectal cancer. Among the endothelial markers, CD34 demonstrated the most consistent correlation with tumor grade and prognosis, while CD105 reflected active neovascularization in invasive fronts. Elevated VEGF expression was observed in approximately 70% of CRC specimens and was associated with reduced disease-free and overall survival. Hypoxia-inducible factor-1α (HIF-1α) was found to promote VEGF transcription under hypoxic microenvironments, further enhancing angiogenesis and tumor resilience. Several studies confirmed that patients with high VEGF or MVD levels responded poorly to standard chemotherapy but showed partial benefit from anti-angiogenic agents such as bevacizumab and aflibercept. However, inter-study heterogeneity in staining protocols and scoring systems remains a major limitation for standardization.

Conclusion

Angiogenesis represents a pivotal event in colorectal cancer progression and metastasis. Quantitative assessment of MVD and angiogenic biomarkers such as VEGF, CD34, and CD105 provides valuable prognostic information beyond conventional histopathological parameters. The integration of angiogenic profiling into diagnostic practice may refine risk stratification and therapeutic decision-making. Furthermore, combining anti-angiogenic therapy with immunotherapy and cytotoxic agents holds promise for improving survival outcomes. Future multicenter studies should focus on developing standardized protocols for MVD evaluation and identifying predictive markers for responsiveness to anti-angiogenic treatment.

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