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Perspective

Liquid Biopsy Monitoring of Minimal Residual Disease in Early-Stage Colorectal Cancer

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DESCRIPTION

Colorectal cancer is one of the leading causes of cancer related morbidity and mortality worldwide. Despite advances in surgical techniques and adjuvant therapies, recurrence remains a significant concern, even in patients with early stage disease. Minimal residual disease refers to the small population of cancer cells that remain in the body after curative treatment and are often undetectable using conventional imaging techniques or laboratory markers. These residual cells can give rise to disease relapse and metastasis, representing a critical challenge in the management of colorectal cancer. Liquid biopsy, a non invasive method of analyzing circulating tumour components in the blood, has emerged as a promising tool for monitoring minimal residual disease and guiding personalized therapeutic strategies.

Liquid biopsy involves the collection of a blood sample and the detection of circulating tumour DNA, which consists of fragments of Deoxyribonucleic Acid (DNA) released by cancer cells into the bloodstream. These DNA fragments carry the genetic alterations present in the tumour, including point mutations, insertions, deletions, and structural rearrangements. Because circulating tumour DNA originates from multiple regions of the primary tumour and potential micrometastatic sites, it provides a comprehensive and dynamic picture of tumour burden and genetic heterogeneity. In early stage colorectal cancer, monitoring circulating tumour DNA after surgical resection and adjuvant therapy can reveal the presence of minimal residual disease before clinical or radiological evidence of recurrence becomes apparent.

The clinical utility of liquid biopsy in early stage colorectal cancer has been demonstrated in several studies. Patients with detectable circulating tumour DNA following surgical resection are at significantly higher risk of disease recurrence compared to those without detectable circulating tumour DNA. Longitudinal monitoring of circulating tumour DNA allows clinicians to stratify patients according to risk, enabling the timely initiation of additional therapy for those at highest risk. This approach represents a paradigm shift from traditional surveillance, which relies on periodic imaging and laboratory markers that often fail to detect microscopic residual disease until relapse is clinically evident.

The sensitivity and specificity of liquid biopsy for minimal residual disease detection are influenced by several factors, including the method of circulating tumour DNA analysis, sample handling, and tumour biology. Highly sensitive techniques such as digital polymerase chain reaction and next generation sequencing allow the detection of low abundance mutations in the bloodstream, enabling early identification of residual disease. Standardization of pre analytic procedures, including blood collection, processing, and storage, is essential to ensure reliable and reproducible results. Furthermore, the selection of tumour specific mutations for monitoring enhances the precision of minimal residual disease detection and reduces the risk of false positive results.

One of the unique advantages of liquid biopsy is its ability to capture tumour evolution and emerging resistance mechanisms. Colorectal cancer cells can acquire new genetic alterations during and after therapy, which may contribute to disease progression or recurrence. By sequencing circulating tumour DNA at multiple time points, clinicians can identify newly acquired mutations and adapt treatment strategies accordingly. This dynamic monitoring enables the implementation of precision oncology approaches, where therapy is guided not only by baseline tumour characteristics but also by the evolving molecular landscape of the cancer.

In addition to circulating tumour DNA, other circulating biomarkers such as circulating tumour cells and extracellular vesicles are being investigated for minimal residual disease monitoring. Combining multiple analytes may improve the sensitivity and predictive power of liquid biopsy and provide complementary information about tumour biology, immune interactions, and metastatic potential. Integrating these markers with clinical, pathological, and imaging data can create a comprehensive framework for risk assessment and treatment planning in early stage colorectal cancer.

The translation of liquid biopsy into routine clinical practice requires careful validation in prospective trials and the

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establishment of standardized protocols. Several ongoing clinical studies are evaluating the use of circulating tumour DNA to guide adjuvant therapy, monitor recurrence, and predict long term outcomes in colorectal cancer. Early results are promising, demonstrating that liquid biopsy based strategies can improve relapse detection, reduce unnecessary chemotherapy, and provide actionable molecular insights for personalized treatment. Regulatory approval and reimbursement considerations are also critical to ensure broad access and implementation in diverse healthcare settings.

Despite its promise, challenges remain in the widespread adoption of liquid biopsy for minimal residual disease monitoring. Low levels of circulating tumour DNA in some patients may limit sensitivity, particularly in very early stage disease. Biological variability, including differences in tumour shedding and clearance, can affect the interpretation of results. Additionally, the integration of liquid biopsy into existing clinical workflows requires education and training of healthcare providers, as well as the development of decision support tools to translate molecular findings into actionable treatment plans. Continued research and technological innovation are essential to overcome these limitations and maximize the clinical impact of liquid biopsy.

CONCLUSION

Liquid biopsy offers a transformative approach to the management of early stage colorectal cancer by enabling the detection and monitoring of minimal residual disease. It provides a non invasive, dynamic, and precise assessment of tumour burden, allowing for risk stratification, individualized adjuvant therapy, and early detection of recurrence. By capturing tumour heterogeneity and evolution, liquid biopsy supports the implementation of precision oncology strategies that optimize treatment efficacy and improve patient outcomes. As clinical validation progresses and standardized protocols are established, liquid biopsy is poised to become a central tool in the post surgical management of colorectal cancer, ultimately reducing recurrence rates and enhancing survival for patients with early stage disease.