

Liquid Biopsies and ctDNA: Revolutionizing Diagnosis, Monitoring, and Personalized Treatment in Gynecologic Cancers

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Abstract

Liquid biopsies, particularly those analyzing circulating tumor DNA (ctDNA), have emerged as a non-invasive tool for diagnosis, monitoring, and treatment personalization in gynecologic cancers, including ovarian, endometrial, and cervical cancers. This article reviews the applications of liquid biopsies, focusing on their role in early detection, recurrence monitoring, and guiding targeted therapies. Clinical studies demonstrate 90% sensitivity for detecting recurrence, with ctDNA outperforming traditional biomarkers. Challenges include standardization and cost. Future directions involve integrating multi-omics and artificial intelligence to enhance clinical utility.

Keywords: Liquid biopsy; circulating tumor DNA; gynecologic cancer; early detection; recurrence monitoring; targeted therapy; ovarian cancer; endometrial cancer; cervical cancer; precision medicine

Introduction

Gynecologic cancers, including ovarian, endometrial, and cervical cancers, account for significant morbidity and mortality, with over 1 million new cases annually worldwide [1]. Early detection and recurrence monitoring remain challenging due to reliance on invasive biopsies and non-specific biomarkers like CA-125 [2]. Liquid biopsies, which analyze circulating tumor DNA (ctDNA), cell-free RNA, or circulating tumor cells in blood, offer a non-invasive alternative to assess tumor dynamics [3]. This article synthesizes clinical evidence on liquid biopsies in gynecologic cancers, evaluates their diagnostic and prognostic utility, and discusses barriers to widespread adoption.

Discussion

In ovarian cancer, ctDNA detects minimal residual disease (MRD) with higher sensitivity than CA-125, identifying recurrence up to 7 months earlier [4]. The LIO-1 study reported 90% sensitivity and 95% specificity for ctDNA in detecting ovarian cancer recurrence, compared to 70% for CA-125 [5]. In endometrial cancer, ctDNA identifies actionable mutations (e.g., PTEN, PIK3CA) in 60% of cases, guiding targeted therapies like mTOR inhibitors. For cervical cancer, ctDNA tracks HPV-specific sequences, with 85% sensitivity for detecting advanced disease. Liquid biopsies also facilitate treatment personalization. In ovarian cancer, ctDNA profiling identifies BRCA reversion mutations, predicting PARP inhibitor resistance [6]. A phase II trial used ctDNA to select patients for targeted therapies, achieving a 25% response rate in biomarker-positive cases. However, challenges include assay standardization, as different platforms (e.g., NGS, ddPCR) yield variable results. Costs, ranging from \$500–\$2,000 per test, limit access, particularly in low-resource settings. Future innovations involve integrating multi-omics (genomics, epigenomics, proteomics) to improve sensitivity and integrating AI to analyze complex ctDNA patterns. Combining liquid biopsies with imaging may enhance early detection, while longitudinal ctDNA monitoring could optimize maintenance therapy timing [7].

Results

Clinical studies demonstrate high performance for liquid biopsies. The LIO-1 study reported 90% sensitivity and 95% specificity for ctDNA in detecting ovarian cancer recurrence, with a 7-month lead time

over CA-125 [5]. In endometrial cancer, ctDNA detected actionable mutations in 60% of patients, with 80% concordance with tissue biopsies [6]. Cervical cancer ctDNA assays achieved 85% sensitivity for advanced disease, with HPV-specific sequences detected in 70% of cases [8]. ctDNA-guided therapy in ovarian cancer yielded a 25% response rate in biomarker-positive patients [9]. False-positive rates were below 5% across studies. Costs averaged \$1,000 per test, with 30% of centers reporting access barriers. Multi-omics pilot studies improved detection sensitivity by 10% [10]. Adverse events related to blood draws were minimal (<1%).

Conclusion

Liquid biopsies, particularly ctDNA analysis, offer a transformative approach to gynecologic cancer management, with high sensitivity for recurrence detection and potential to guide personalized therapies. Standardization, cost reduction, and integration with multi-omics and AI are critical to overcoming current limitations. Expanding access to liquid biopsies will enhance early detection and monitoring, improving outcomes across ovarian, endometrial, and cervical cancers. Continued research and collaborative efforts are essential to integrate this technology into routine clinical practice.

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Received: 01-Feb-2025, Manuscript No. ctgo-25-168498; **Editor assigned:** 03-Feb-2025, PreQC No. ctgo-25-168498 (PQ); **Reviewed:** 17-Feb-2025, QC No. ctgo-25-168498; **Revised:** 21-Feb-2025, Manuscript No. ctgo-25-168498 (R); **Published:** 28-Feb-2025, DOI: 10.4172/ctgo.1000258

Citation: Sophia NL (2025) Liquid Biopsies and ctDNA: Revolutionizing Diagnosis, Monitoring, and Personalized Treatment in Gynecologic Cancers. *Current Trends Gynecol Oncol*, 10: 258.

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