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Assessment of preoperative and postoperative circulating cell free tumour DNA (ctDNA) can predict risk of recurrence in patients with nonmetastatic breast cancer

Fara Hassan^{1,2}, Jiang Huai Wang²,
Donal Peter O'Leary^{1,2}, Carolyn Cullinane^{1,2},
Mark Corrigan^{1,3}, Henry Paul Redmond^{1,2}

¹Department of Breast Surgery, Cork University Hospital, Cork, Ireland; ²Department of Breast Surgery, University College Cork, Cork, Ireland; ³SURGUANT Research Lab, University College Cork, Cork, Ireland

Background: Postoperative risk stratification in nonmetastatic breast cancer presents ongoing challenges. Circulating tumour DNA (ctDNA) contains tumour-specific gene mutations detectable in the blood of patients with breast cancer. In this study, we investigated the feasibility of High-Resolution Melting (HRM) PCR technology for detecting PIK3CA mutations in preoperative and postoperative blood samples and its prognostic significance in patients with breast cancer.

Methods: Preoperative and postoperative blood samples were analysed from 63 patients with breast cancer who underwent curative surgery. HRM PCR was used to identify PIK3CA mutations at exon 9 and 20 in ctDNA. HRM assays were developed using specifically designed primers and genomic DNA isolated either from cell lines or ctDNA. Melting curve analyses and mutation analyses were performed on the Light Cycler PCR platform.

Results: In a cohort of 63 patients [age, median interquartile range (IQR), 52 years (26–84 years)], with a median follow-up of 60 months (IQR, 3–60 months), 26 (41.2%) and 22 (35%) patients had detectable PIK3CA mutations in ctDNA preoperatively and postoperatively, respectively. Detectable PIK3CA mutations in postoperative ctDNA [hazard ratio (HR): 4.95, 95% confidence interval

(CI): 1.87–13.09, P=0.0003] was associated with inferior recurrence-free survival (RFS). ctDNA-based detection preceded clinical detection of recurrence (n=13,35%) in patients with positive metastasis with an average lead time of 16 months (range, 12–24 months)

Conclusions: Our study highlights the prognostic significance of ctDNA in preoperative and postoperative serum samples of patients with breast cancer. However, prospective studies are needed to assess the prognostic potential of ctDNA in patients with non-metastatic breast cancer.

Keywords: Circulating tumour DNA (ctDNA); breast cancer; preoperative period (preop); postoperative period (postop); recurrence

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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