Enumeration of circulating tumor cell (CTC) clusters as a function of age or neutrophil -to-lymphocyte-ratio (NLR) in women with metastatic breast cancer.

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Introduction

CTC clusters are established mediators of metastasis in breast cancer and are associated with unfavorable clinical outcomes. However, their prevalence and phenotypic characteristics in older patient populations remain inadequately studied. Systemic inflammation, as measured by the NLR, may influence CTC dynamics.

Material & methods

A prospective translational analysis was conducted in women with metastatic breast cancer (mBC), stratified into two cohorts: **Group A (age ≥70 years)** and **group B (age <70 years)**. Peripheral blood samples were processed using the FDA-cleared Parsortix® system for CTC enrichment, followed by immunofluorescence staining (EpCAM/HER2/EGFR/CD45) to identify single CTCs and CTC clusters (homotypic and heterotypic). Baseline clinical characteristics, including histological subtype, stage, tumor grade, Ki-67 index, and sites of metastasis, were documented. NLR ≥4 was defined as elevated. Primary endpoints included CTC cluster frequency and size; secondary endpoints assessed correlations with age group and NLR status.

Discussion & Conclusion

While older patients with mBC (Group A) exhibited a trend for higher systemic inflammation as indicated by NLR, no statistically significant differences in CTC cluster frequency or size were observed compared to younger patients (Group B). Moreover, elevated NLR was not independently predictive of increased cluster prevalence. These findings underscore the need for further investigation into age-associated CTC phenotypes and their potential clinical implications in larger patient populations.

Results

A total of 155 patients were evaluable, including 58 patients in group A (mean age: 78 years). A trend for elevated NLR being more frequent in Group A compared to Group B was visible (53.2% vs 36.8%, P = 0.075). No statistically significant differences were observed between groups regarding histological subtype, stage at diagnosis, or tumor grade. The Ki-67 proliferation index was significantly elevated in group B (mean 37%) compared to Group A (mean 21%, P < 0.001). The pattern of metastatic spread was comparable, although a trend toward increased brain metastases was observed in Group B. A trend showing a higher proportion of patients exhibiting ≥1 CTC in Group B was detected (43.5% vs. 29.3%, P = 0.082). CTC clusters were identified in 6.9% of Group A and 12.5% of Group B (P = 0.275). Elevated NLR (≥4) was not significantly associated with CTC cluster presence (11.1% vs. 8.2%, P = 0.594)

Figure 1: CTCs capture

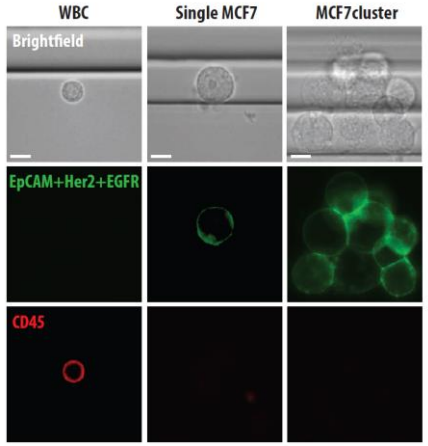
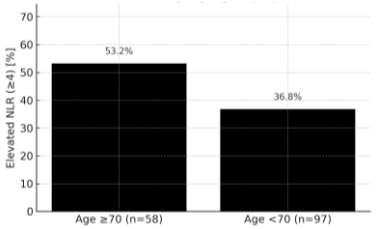


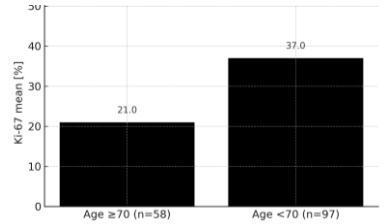
Figure 1: Representative images of a captured MCF7 single cell, a cell cluster (green) and a contaminant white blood cell (WBC; red) in the Parsortix microuidic cassette

Figure 2A-D:

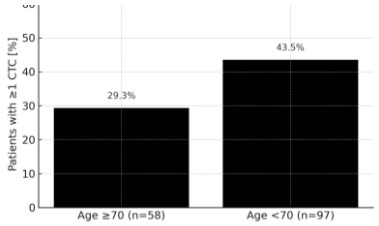
A: Elevated NLR by age group



B: Ki-67 proliferation index by age group



C: ≥1 CTC detected by age group



D: CTC clusters by age group

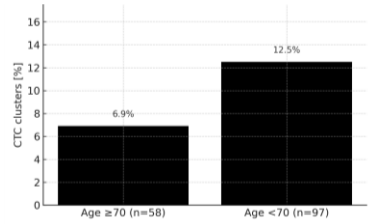


Figure 2:
(A) Frequency of elevated NLR (≥4) by age group.
(B) Mean Ki-67 index in age ≥70 vs <70.
(C) Proportion of patients with ≥1 detectable CTC.
(D) Prevalence of CTC clusters by age group.

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