

A liquid biopsy-based method for the detection and quantification of circulating tumor cells in surgical osteosarcoma patients

Zhen Wang, MD, PhD¹, Haoqiang Zhang, MD¹, Ling Wang, MD, PhD²

¹*Department of Orthopedics, Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi, P. R. China, 710032*

²*Department of Vascular and Endocrine Surgery, Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi, P. R. China, 710032*

Abstract

Objective: To develop a method for the quantification of circulating tumor cells (CTCs) in osteosarcoma (OS) and prospectively validate the method in a cohort of surgical OS patients.

Summary background data: No method for the enumeration and quantification of OS CTCs is currently available. A relationship between the number of CTCs and progression-free survival has been established in other types of cancer, and may apply to OS CTCs as well.

Methods: OS CTCs were enumerated from spiked human peripheral blood (PB) following erythrocyte and leukocyte depletion. The CTCs were quantified microscopically based on aneuploidy and a CD45⁻ phenotype. Aneuploidy was assayed by interphase fluorescence in situ hybridization (iFISH) using fluorescence-labeled alpha-satellite probes for the centromeres of chromosome (CEP 8). CD45 phenotyping was performed with immunocytochemistry. The same protocol was applied to liquid biopsies derived from a cohort of surgical patients with primary and recurrent/metastatic OS. The number of CTCs were correlated to progression-free survival (PFS).

Results: PB of recurrent/metastatic OS patients contained more CTCs than the PB of primary OS patients. OS patients with ≥ 2 CTCs per 7.5 mL of PB had worse PFS than patients whose PB contained < 2 CTCs.

Conclusions: The iFISH/immunocytochemistry method was suitable to quantitate CTCs in liquid biopsies of OS patients. The number of CTCs in liquid biopsies have prognostic value.

Keywords

CTC enumeration, interphase fluorescence in situ hybridization, progression-free survival, personalized medicine