AIMS Medical Science

AIMS Medical Science, 9(1): 5–8.
DOI: 10.3934/medsci.2022002
Received: 01 September 2021
Revised: 09 January 2022
Accepted: 09 January 2022
Published: 11 January 2022

http://www.aimspress.com/journal/medicalScience

Letter

Reduction of blood cofilin-1 in cancer patients treated with radiotherapy

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Dear Editor,

The prognosis of radiotherapy is important for evaluating therapeutic efficacy. As the patient survival rate requires tracking for several years, early diagnosis of appropriate biomarkers may benefit from predicting the results of radiotherapy. This study focused on the expression of cofilin-1, which is a member of the actin depolymerizing factor (ADF)/cofilin family in the blood samples of cancer patients [1,2], including prostate cancer, lung cancer, nasopharyngeal carcinoma, pancreatic cancer, thymic cancer, and endometrial carcinoma. Blood samples were collected before and after radiotherapy with or without other adjuvant treatments, such as target therapy, anti-hormone therapy, and chemotherapy, for one month and three months. The blood cofilin-1 was extracted from the buffy coat and analyzed using the Enzyme-Linked Immunosorbent Assay (ELISA). Blood samples were donated from 29 patients recruited from Taipei City Hospital, RenAi Branch, Taiwan. In addition, 466 healthy volunteers were recruited for comparison. This study is based on the approval of the institutional review board of this hospital (TCHIRB-10510103 and TCHIRB-10409111). The National Comprehensive Cancer Network® (NCCN®) Guidelines (https://www.nccn.org/guidelines/category_1) were used as the criteria for patients at different clinical stages to be assigned for radiotherapy [3]. The linear accelerators (LINAC) used in the hospital include Elekta Infinity and Elekta Synergy (Elekta Solutions AB, Stockholm, Sweden). All cancers were

irradiated using the technique of Volumetric Modulated Arc Therapy (VMAT), and the dose rate was 400–600 MU/min. It was found that the level of cofilin-1 was approximately 3-fold up-regulated in the blood samples of the various cancer patients, as compared to the healthy controls (Figure 1A). After radiotherapy, the blood cofilin-1 levels of all cancer patients were down-regulated for up to three months (Figure 1B). Regarding the one-month and three-month follow-ups after radiotherapy, the latter showed that the blood cofilin-1 level was significantly recovered; however, the level was still lower than that of pre-radiotherapy (Figure 1C and 1D). While there was no significant difference between one and three months post-radiotherapy at different cancer stages, the cancers without lymphatic migration exhibited a significant recovery of blood cofilin-1 levels after three months of radiotherapy (Figure 1E). While the total expression of the blood cofilin-1 level in 19 breast cancer patients was similar to the total of the cancer patients before and after radiotherapy, a significant recovery of blood cofilin-1 was found in Her2 positive and Ki-67 positive groups after three months of radiotherapy (Figure 1F and 1G). Furthermore, the receiver operating characteristic (ROC) curve analysis showed that the area under the curve (AUC) of the reduced blood cofilin-1 level was 0.87 and 0.8 after radiotherapy for one month and three months, respectively (Figure 1H and 1I). Thus, the current data suggest that the blood cofilin-1 level may be used to evaluate the response to radiotherapy. However, the limitations of this study include a small sample size, adjuvant radiotherapy, multiple cancer types, and short post-therapeutic tracking time, thus, it is difficult to compare the therapeutic outcomes of various cancers. As breast cancer patients accounted for most samples in this study, it is interesting to further focus on the correlation of radiotherapy and the reduction of blood cofilin-1 levels in breast cancer patients. In summary, the reduction of blood cofilin-1 may be a prognostic biomarker or early responder of radiotherapy. The clinical implications of this phenomenon should be addressed in the future.

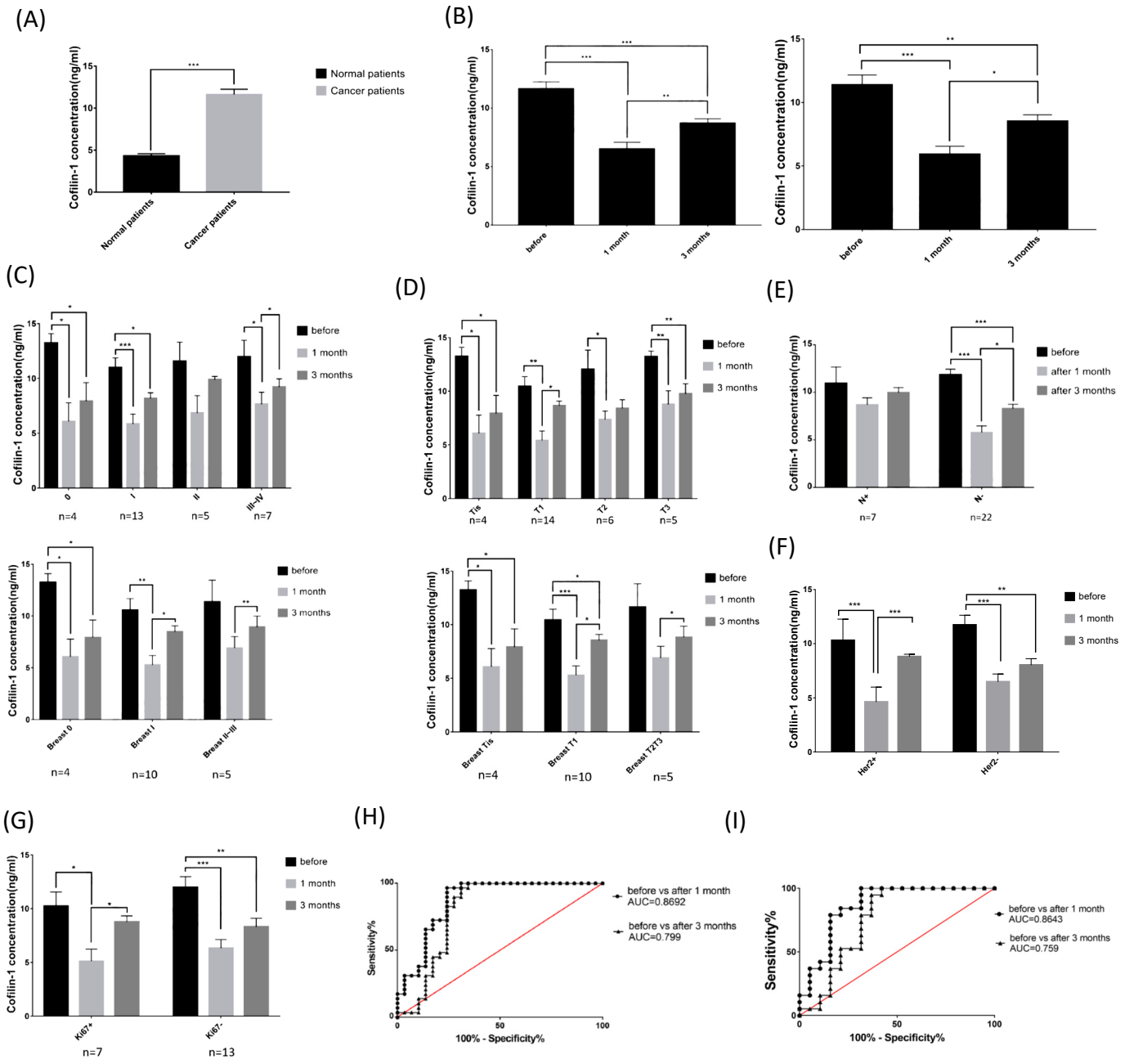

Figure 1. Reduction of blood cofilin-1 after radiotherapy. (A) Comparison of blood cofilin-1 levels of healthy controls and cancer patients. (B) Analysis of blood cofilin-1 in all cancer patients (left panel) and before and in breast cancer patients (right panel) after radiotherapy for 1 and 3 months. (C) Blood cofilin-1 level in different stages of cancer patients (upper panel) and that of breast cancer patients (lower panel) before and after radiotherapy. (D) Blood cofilin-1 level in TNM staging of all cancer patients (upper panel) and that of breast cancer patients (lower panel) before and after radiotherapy. (E) Comparison of blood cofilin-1 in cancer patients with or without lymph node metastasis. (F) and (G) Comparison of blood cofilin-1 in breast cancer patients with Her2 positive or Her2 negative, and Ki-67 positive or Ki-67 negative before and after radiotherapy, respectively. (H) and (I) The ROC curve analysis for reduced blood cofilin-1 after radiotherapy in all cancer patients and in breast cancer patients, respectively. *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$.

Acknowledgement

This study was supported by Taipei City Hospital (TPCH-106-011), and a grant from Ministry of Science and Technology of Taiwan (109-2314-B-010-021-MY3). We thank the administrative assistance from Ms. Ya-Huai Wang. The publication related fees, if any, was supported by the Ministry of Science and Technology of Taiwan (109-2314-B-010-021-MY3).

Conflict of interest

The authors declare that there are no conflicts of interest.

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