



Albumin to fibrinogen ratio and fibrinogen to pre-albumin ratio are economical, simple and promising prognostic factors for solid malignancy

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The exploration of cancer prognostic factor has received increasing attention in recent years. Traditional indicators such as tumor-node-metastasis system, histological subtype and carcinoembryonic antigen (CEA) have been recognized as prognostic indicators. However, invasiveness and high cost of these factors restrict the widespread use in clinic, particularly in economically underdeveloped basic health units. Therefore, economic, simple and effective biomarkers are warranted to manage and improve prognosis of cancer individuals.

In recent decades, chronic inflammation and malnutrition are two research hotspots in onset and progression of cancer. Chronic inflammation promotes carcinogenesis, chemoresistance as well as regional or distal metastasis (1). Malnutrition damages the anatomic barriers, immunity and other defense mechanisms (2). Some inflammation-based factors such as glasgow prognostic score, neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) have been extensively evaluated for prognosis in many kinds of malignancy. However, cancer patients with the same level of them show the obvious heterogeneous survival.

Our study detected circulating neutrophil, lymphocyte, monocyte, platelet, fibrinogen (Fib), albumin (Alb), and pre-albumin (pAlb), which were candidate factors reflecting the status of chronic inflammation and malnutrition, to investigate the prognostic roles of them in each stage (early- and advanced-stage) of lung cancer, esophageal squamous cell carcinoma (ESCC), colorectal cancer (CRC), gastric cancer (GC) and hepatocellular cancer (HCC), respectively.

Fortunately, our study found that the patient with lower Alb-to-Fib ratio (AFR) was significantly associated with increased death risk for early- and advanced-stage non-small cell lung cancer (NSCLC) as well as 0-III stage ESCC (3,4). AFR was significantly associated with tumor size and the death predicted efficacies were higher than NLR, PLR and monocyte-lymphocyte ratio in the two kinds of malignancy. Moreover, Fib to pAlb ratio (FPR) was observed to be a promising prognostic biomarker for II-III stage GC, HCC and II-IV stage CRC, respectively (5-7), and the predicted efficacies of AFR and FPR based scores (ADS and CCF) for ESCC and CRC patients were superior to the single biomarker (3,7). AFR, FPR

and the novel scores could stratify the patient with GC, CRC, HCC and NSCLC who may benefit from single chemoradiotherapy, adjuvant chemoradiotherapy after surgical resection as well as target therapy (4-7). For instance in one of above studies (4), we found that clinical outcome of high AFR patient with chemo-radiotherapy was superior to low AFR patient; overall survival rate of stage II-III NSCLC patients undergoing chemo-radiotherapy was significantly lower than the surgical patients with treatment of adjuvant chemo-radiotherapy in low AFR subgroup. On the contrary, clinical outcome of the patients receiving chemo-radiotherapy was the same to the patients undergoing surgery and adjuvant chemo-radiotherapy in high AFR subgroup. Thus, it's easy for us to conclusion that surgical resection plus chemo/radiotherapy and single adjuvant chemo/radiotherapy are more suitable for advanced NSCLC patients with low and high AFR, respectively. Additionally, our team also confirmed that constant detection of circulating FPR could monitor the progression of advanced CRC (8). Meanwhile, both AFR and FPR could be considered as novel diagnostic biomarkers to discriminate gallbladder carcinoma and CRC from the benign disease and healthy individuals, respectively (9,10).

It is the first time for us to report the prognostic roles of AFR and FPR in stage II-III GC in March of 2017. Subsequently, lots of the following studies were reported. More interestingly, these studies achieved the consistent conclusion that AFR was an independent prognostic factor for NSCLC, soft tissue sarcoma, gallbladder cancer, chronic lymphocytic leukemia, prostate cancer, breast cancer and high-grade gliomas, respectively (11-17). Additionally, Hamanaka and coworkers affirmed AFR as an economic, simple and effective biomarker for lung cancer in the editorial on our article (18). As we known, Fib is not only an essential component of coagulation cascade, but also is an acute-phase reactant reflecting the status of systemic inflammation. Previous researches reported that hyperfibrinogenemia was associated with cancer metastasis (19). High inflammation-induced interleukin-6 in cancerous cells and tumor-released other inflammatory factors such as fibroblast growth factor-2 (FGF-2), vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) interacted with stromal cell and inflammatory cell to trigger high-expression of Fib(20). Alb and pAlb are recognized as both nutritional indicator and response biomarker of systemic inflammation. Malnutrition impairs the immune system, increases probability of

infection and promotes the progression of malignancy by accelerating systemic inflammation. In accordance with our findings and the above studies, we believe that AFR and FPR are practical and effective biomarkers to manage and predict the clinical outcome of patients with solid malignancy. We also believe that such effect of these biomarkers on cancer prognosis may be highly influenced by the number of prediction potential cells. It is our another focus to further study that potential cells are related to these indicators.

In summary, AFR and FPR are two economical, simple and effective independent biomarkers to monitor progression of solid malignancies and to predict prognosis as well as to guide the patients to precisely receive the optimal therapeutic regimen.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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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