Reply to “Letter to the editor: Intravital imaging of the association between intravascular neutrophil extracellular traps and microvascular obstruction using multiphoton microscopy”

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REPLY: We thank Dr. Tanaka and colleagues (11) for their comments on our article published in the American Journal of Physiology-Heart and Circulatory Physiology, entitled “Neutrophil extracellular traps in ischemia/reperfusion injury-induced myocardial no-reflow: therapeutic potential of DNase-based reperfusion strategy” (6).

Emerging evidence suggests a potential contribution of neutrophil extracellular traps (NETs) in linking sterile inflammation and thrombosis (4, 7, 12). We and others (6, 9) recently demonstrated the existence of NETs after myocardial ischemic challenge and confirmed the therapeutic potential of NET-targeted interventions in ameliorating myocardial ischemia/reperfusion injury. Additionally, we hypothesized that the formation of NETs may be associated with coronary microcirculation obstruction, which is a major reason leading to coronary “no-reflow” phenomenon in clinical practice. To this end, we used thioflavin S and Evans blue staining, a classical method for detecting the anatomic no-reflow in experimental research, which revealed that DNase I combined with tissue-type plasminogen activator (a thrombolytic agent) could reduce anatomic no-reflow area.

In Tanaka and colleagues’ recent work (10), with the aid of two photon laser-scanning microscopy, they observed two forms of intravascular NETs, i.e., circulating cell-free NETs and anchored NETs, in various organs of lipopolysaccharide-challenged mouse model, and they noted reduced intravascular NETs by DNase in real time. Therefore, they suggested the use of intravital imaging technique in the investigation of NET-mediated myocardial microcirculation obstruction and coronary no-reflow (11).

We totally agree with Dr. Tanaka and colleagues’ invaluable suggestion and highly appreciate their elegant work in the field of NET-mediated thrombosis (10). The intravital imaging technique should be incorporated in future studies to evaluate the dynamics of coronary NET formation, which may provide important information for translational purpose in humans, such as the time frame for effective interventions.

Since the first publication of NETs as a novel innate defense mechanism against infections in 2004 (2), the past decade has witnessed growing interest of the participation of NETs in varieties of disease processes. Enlightened by the pioneer work by Wagner’s group (5), mounting evidence suggests a critical role of NETs in human coronary heart disease (1, 3). Notably, a recent work demonstrated that coronary NET burden in patients suffering acute ST-elevation coronary syndrome is an independent predictor for increased infarct size (8). Thus these findings undoubtedly open a new avenue for basic and translational researches for NET-targeted interventions in acute coronary syndrome, one of the leading causes of morbidity and mortality worldwide.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS


REFERENCES


