Editorial

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Hepcidin and Neutrophil Gelatinase-Associated Lipocalin as a Biomarker for Acute Kidney Injury Linked Iron Metabolism

Acute kidney injury (AKI) is one of the serious complications of cardiac surgery and can be a significant life-threatening factor associated with high morbidity and mortality [1-3]. There are multiple damaging mechanisms of cardiac surgery-induced AKI, such as ischemia and reperfusion injury, inflammation, and oxidative stress [4]. Among various candidate biomarkers and underlying mechanisms, hepcidin and iron metabolism in AKI are recently attracting the attention of researchers as one of the main mechanisms causing renal damage in various clinical conditions [5-9]. However, the role of iron regulation in cardiac surgery still remains unclear [8].

Hepcidin is mainly synthesized in the liver; however, lower hepcidin expression has also been identified in the kidneys [1, 6]. The main biological role of hepcidin is as an essential regulator of iron metabolism [1, 2, 6]. Hemoglobin, myoglobin, cytochromes, and various enzymes need iron as an important component of their functions [1]. However, excessive iron accumulation and extracellular free-iron can cause tissue injury [1]. Therefore, human body requires delicate and efficient tools to control iron absorption and excretion not only to maximize physiologic iron utility but also to minimize undesirable toxicity [1]. Hepcidin appears to downregulate iron absorption in duodenum and reduce extracellular iron levels [1, 2]. Therefore, hepcidin is known to be a major regulator of iron homeostasis resulting in intracellular iron sequestration [6]; its deficiency induces iron-overload disease such as hereditary hemochromatosis, while its excess results in anemia such as anemia of chronic disease [1].

Besides iron status, two other mechanisms regulate hepcidin levels:erythropoietic activity and systemic inflammation. Hepcidin is downregulated by hypoxia-induced erythropoiesis and upregulated by interleukin (IL)-6 mediated systemic inflammatory reaction [1, 5]. These multiple mechanisms involving hepcidin metabolism can make clinical interpretation difficult in renal injury.

To avoid injury due to ferroptosis, various iron binding proteins serve as endogenous protective molecules through sequestering labile iron [2, 9]. Neutrophil gelatinase-associated lipocalin (NGAL) is a well evaluated AKI biomarker with a broad spectrum of etiology [3]. Interestingly, NGAL as well as hepcidin are involved in iron metabolism as iron sequestering components [1, 6, 9]. Upregulation of NGAL can be detected in both plasma and urine early after AKI, suggesting possible renal protective mechanism through iron sequestration [2]. Both NGAL and hepcidin show iron sequestering function with different mechanisms [6].

In this issue, Albert, *et al*. [4] reported a pilot evaluation of various urinary AKI biomarkers linked to iron metabolism and inflammation. They suggested that NGAL, hepcidin, NGAL/hepcidin ratio, and IL-6 were independent predictors of AKI after an open heart surgery [4]. This pilot study may be an interesting precedent for understanding the role of iron metabolism through hepcidin and NGAL in AKI. We expect similar investigations will

increase both in larger patient groups and in various phenotypes of AKIs, to further elucidate the clinical utility of these biomarkers.

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Author contribution

Both authors equally contributed as a corresponding author.

Conflict of interest

Nothing to declare.

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