Editorial

Ann Lab Med 2021;41:355-356
https://doi.org/10.3343/alm.2021.41.4.355
ISSN 2234-3806 • eISSN 2234-3814

ANNALS OF LABORATORY MEDICINE

Sun Young Cho, M.D., Ph.D. [1] and Mina Hur, M.D., Ph.D.[2]

[1]Department of Laboratory Medicine, Kyung Hee University Hospital, Seoul, Korea; [2]Department of Laboratory Medicine, Konkuk University School of Medicine, Seoul, Korea

Hepcidin-25 as a Novel Kidney Biomarker for Cardiac Surgery-Associated Acute Kidney Injury

Acute kidney injury (AKI) is the most common and clinically important complication in patients undergoing cardiac surgery, showing stage-dependent worsening of prognosis [1, 2]. Several pathophysiological mechanisms may simultaneously induce cardiac surgery-associated AKI (CSA-AKI) even in one patient, including renal ischemia–reperfusion injury, inflammation, oxidative stress, hemolysis, iron metabolism, and nephrotoxins; accordingly, any single urinary biomarker cannot satisfy every requirement regarding the underlying pathophysiological mechanisms [1, 2]. Multiple pathophysiological backgrounds naturally require combinations of multiple biomarkers as a necessity. Recently, various novel biomarkers have favored the assessment of CSA-AKI in addition to the conventional tests. The biomarkers, such as urinary liver fatty acid binding protein (L-FABP), urinary neutrophil gelatinase-associated lipocalin (NGAL), serum L-FABP, heart-type FABP, kidney injury molecule 1 (KIM-1), and interleukin-18 were found to be significantly higher in patients with CSA-AKI than in those without [3]. Because kidney replacement therapy (KRT) should be done as soon as possible in order to get promising outcomes in patients with CSA-AKI, combining novel biomarkers may help predict the diagnosis, adverse outcomes, and mortality due to CSA-AKI [2, 3].

In this issue, Albert C, et al [4] reported that plasma NGAL:hepcidin-25 is a promising marker for predicting postoperative major adverse kidney events after cardiac surgery. In their previous study, considering laboratory and clinical availability of the biomarkers, they concluded that NGAL and interleukin-6 appear to be the most excellent candidates for implementation in kidney risk assessment [2]. Moreover, they suggested that the combination of biomarkers with hepcidin-25 may further improve diagnostic discriminations [2]. Hepcidin-25 is an iron-sequestering protein associated with AKI, and it has renoprotective functions when exogenously administered in animal models [5]. Because of the inverse association between hepcidin-25 and the development of CSA-AKI, it is speculated that its endogenous renoprotective mechanism is due to sequestation of catalytic free iron released during surgery with a significant decrease in kidney tubular injury, apoptosis, oxidative stress, and inflammation, and improved kidney function [5, 6]. Catalytic iron plays a critical role in AKI development, because it makes highly reactive hydroxyl radicals that induce oxidative damage and tubular lipid peroxidation [5, 6]. The renoprotective effect of hepcidin-25 may be mediated through inhibition of ferroptosis, which is an iron-dependent form of cell death that is characterized by tubular lipid peroxidation [5, 6].

In this time, the authors newly presented the roles of plasma NGAL:hepcidin-25 in maintaining the homeostasis of labile-iron during and after cardiac surgery [4]. Consistent with recent reports showing changes of both urinary and plasma hepcidin-25 concentrations, their results also suggested that lower concentrations of hepcidin-25 are independently associated with increased mortality in critically ill patients with AKI requiring KRT [4].

In addition to the various kidney markers mentioned above, there are a broad spectrum of candidate kidney markers that require continuous researches and validations. Continuous efforts to find the best combination of novel kidney biomarkers according to various mechanisms of kidney damage should be made in the future. Among these biomarkers, hepcidin-25 is expected to be a good combination partner with conventional kidney markers in both serum and urine specimens.

CONFLICTS OF INTEREST

No potential conflicts of interest relevant to this article were reported.

REFERENCES

1. Wang Y and Bellomo R. Cardiac surgery-associated acute kidney injury: risk factors, pathophysiology and treatment. Nat Rev Nephrol 2017;13:697-711.
2. Albert C, Haase M, Albert A, Kropf S, Bellomo R, Westphal S, et al. Urinary Biomarkers may complement the Cleveland score for prediction of adverse kidney events after cardiac surgery: a pilot study. Ann Lab Med 2020;40:131-41.
3. Yuan SM. Acute kidney injury after cardiac surgery: risk Factors and novel biomarkers. Braz J Cardiovasc Surg 2019;34:352-60.
4. Albert C, Haase M, Albert A, Ernst M, Kropf S, Bellomo R, et al. Predictive value of plasma NGAL:hepcidin-25 for major adverse kidney events after cardiac surgery with cardiopulmonary bypass: a pilot study. Ann Lab Med 2021;41:357-65.
5. Haase-Fielitz A, Mertens PR, Plass M, Kuppe H, Hetzer R, Westerman M, et al. Urine hepcidin has additive value in ruling out cardiopulmonary bypass-associated acute kidney injury: an observational cohort study. Crit Care 2011; 15: R186.
6. Choi N, Whitlock R, Klassen J, Zappitelli M, Arora RC, Rigatto C, Ho J. et al. Early intraoperative iron-binding proteins are associated with acute kidney injury after cardiac surgery. J Thorac Cardiovasc Surg 2019;157:287-97.e2.

Corresponding author: Sun Young Cho, M.D., Ph.D.
https://orcid.org/0000-0002-3208-5446
Department of Laboratory Medicine, School of Medicine, Kyung Hee University Hospital, 23 Kyungheedae-ro, Dongdaemun-gu, Seoul 02447, Korea
Tel: +82-2-958-8671, Fax: +82-2-958-8609
E-mail: untoyou@hanmail.net

Co-corresponding author: Mina Hur, M.D., Ph.D.
https://orcid.org/0000-0002-4429-9978
Department of Laboratory Medicine, Konkuk University School of Medicine, 120-1 Neungdong-ro, Gwangjin-gu, Seoul 05030, Korea
Tel: +82-2-2030-5581, Fax: +82-2-2636-6764
E-mail: dearmina@hanmail.net

Key Words: Kidney biomarker, Cardiac surgery, Acute kidney injury