Syndecans are transmembrane proteoglycans (PGs) that consist of a core protein to which growth factor binding glycosaminoglycan side chains are attached. Syndecans affect a wide range of physiological processes, and their contribution is most apparent during wound repair. The Syndecan family, transmembrane heparan sulfate PGs, consists of 4 members: Syndecan-1 (Syndecan=the major syndecan of epithelial cells), Syndecan-2 (Fibroglycan=present primarily on cells of mesenchymal origin), Syndecan-3 (N-Syndecan=primarily observed in neuronal tissue and cartilage), and

**Figure.** Major heparan sulfate proteoglycans core protein families. Schematic illustration of structurally related Syndecan genes, showing the 2 subfamilies of syndecans: Syndecan-1 and -3, and Syndecans -2 and -4, respectively. The extracellular domain is highly variable, with the exception of the glycosaminoglycan (GAG) attachment sites, and the proteolytic cleavage site near the plasma membrane. In contrast, the endo- and transmembrane domains are well-preserved. MW, molecular weight; kD, kilodalton.

(Modified with permission from Szatmari T, et al and Rosenberg RD, et al.)

The opinions expressed in this article are not necessarily those of the editors or of the Japanese Circulation Society.

Received May 19, 2015; accepted May 19, 2015; released online June 1, 2015

Department of Cardiovascular Medicine, Kumamoto University Hospital, Kumamoto, Japan

Mailing address: Seiji Hokimoto, MD, PhD, Department of Cardiovascular Medicine, Kumamoto University Hospital, 1-1-1 Honjo, Kumamoto 860-8556, Japan. E-mail: shokimot@kumamoto-u.ac.jp


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Syndecan-4 (Ryudocan/Amphyglycan=ubiquitously expressed)³⁴ (Figure).

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Heart failure (HF) is a common problem with increasingly high rates of mortality and morbidity, and worsening of HF results in multiple re-hospitalizations and excessive healthcare costs. The coexistence of acute kidney injury (AKI) in HF patients leads to poor prognosis, and certain biomarkers that are able to predict AKI onset in the early stage of HF have been identified worldwide. Furthermore, endothelial dysfunction is associated with the development of AKI, and nitric oxide, vascular trophic support, and/or endothelial progenitor cells may be important in ameliorating the acute and/or chronic effects of ischemic AKI.³ It is important to predict and prevent renal worsening because cardiovascular mortality is high in patients with end-stage renal dysfunction.⁵

A recent report showed an association between plasma noradrenaline/adrenaline levels and plasma Syndecan-1 levels in patients with ST-segment elevation myocardial infarction.⁶ That study demonstrated that Syndecan-1 is a biomarker of endothelial glyocalyx damage, and circulating Syndecan-1 levels are elevated in patients with acute myocardial infarction.

Previous studies have revealed that independent predictors for AKI (worsening renal function: WRF) include a history of HF or diabetes mellitus, and admission to hospital of renal dysfunction or hypertension, and a point score based on these characteristics and their relative risk ratios can also identify patients who are at risk for AKI (WRF).⁸ Tromp et al⁹ showed that plasma Syndecan-1 levels correlated with fibrosis markers relating to cardiac remodeling in HF with a reduced ejection fraction, and these levels were associated with clinical outcomes in patients with HF with a preserved ejection fraction.⁹

In this issue of the Journal, Neves et al¹⁰ evaluate the relationship between plasma Syndecan-1 levels and renal dysfunction or mortality in patients with acute decompen- sated HF (ADHF). These researchers determined that plasma Syndecan-1 levels are predictive for an increased risk of developing AKI, in-hospital death, and mortality in the 6-month follow-up. They describes the usefulness of measuring plasma Syndecan-1 levels in ADHF patients and that it is notably valuable in daily clinical practice. It is important to diagnose AKI/WRF in the early stages of HF, and these researchers observed a potent biomarker that could predict an increased risk of AKI in ADHF patients. Importantly, these researchers investigated an endothelial functional marker and assessed not only in-hospital mortality rates but also long-term mortality rates. Moreover, with regard to other endothelial markers, there were no significant relationships between AKI in ADHF and intercellular adhesion molecule-1 or nitrogen oxides. These data are highly valuable, and plasma Syndecan-1 may be a potent useful biomarker in clinical practise.

A further detailed and comparative discussion may be required for the following reasons: if increased plasma Syndecan-1 levels reflect endothelial dysfunction, there may be a relation-ship among plasma Syndecan-1 level, AKI/WRF onset, and certain endothelial function markers, such as the flow-mediated dilation¹¹ test or reactive hyperemia peripheral arterial tonometry.¹² Moreover, an assessment of the amelioration in endothelial function, which clarifies medications, including vasodilators, may also be required. Although these researchers demonstrated the relationships between plasma Syndecan-1 levels and hospital or long-term mortality rates in their study, the mechanism remains unclear. Thus, further pathophysiological discussions, including animal experiments, are warranted. The usefulness of plasma Syndecan-1 levels is expected clinically; thus, verification using large-scale clinical studies is needed.

Finally, Neves et al provide clinically useful and important information for the risk stratification of ADHF patients who might develop AKI/WRF. The authors demonstrated that Syndecan-1 may be a potent useful biomarker in clinical situations, and their study cannot be highly evaluated until it has been published and read widely.

**References**