Unravelling the Complexities of Myocardial Injury in Patients with Chronic Kidney Disease

Fujii, Hideki

(Citation)
Journal of Atherosclerosis and Thrombosis,31(5):522-523

(Issue Date)
2024-05-01

(Resource Type)
journal article

(Version)
Version of Record

The official journal of the Japan Atherosclerosis Society and
the Asian Pacific Society of Atherosclerosis and Vascular Diseases

Editorial

J Atheroscler Thromb, 2024; 31: 522-523. http://doi.org/10.5551/jat.ED256

Unravelling the Complexities of Myocardial Injury in Patients with Chronic Kidney Disease

Hideki Fujii

Division of Nephrology and Kidney Center, Kobe University Graduate School of Medicine, Kobe, Japan

See article vol. 31: 540-549

In patients with chronic kidney disease (CKD), specifically end stage kidney disease (ESKD), incidence of cardiovascular disease (CVD) events and CVD mortality is substantially higher than in the general population[1]. Furthermore, heart failure (HF) is the most common among CVDs in this population[2]. The causes of HF include ischemic heart disease due to coronary artery disease, hypertensive heart disease, and various types of cardiomyopathies. However, pathophysiological mechanisms are highly complex, and details often remain unclear. For example, we sometimes encounter patients who exhibit remarkable pulmonary congestion and globally reduced cardiac systolic function, thus requiring urgent hospitalization for HF. Although coronary angiography is usually conducted for such cases, we often find that patients have no significant coronary artery stenosis. Apart from coronary artery disease, numerous factors, including volume overload, hypertension, diabetes mellitus, anemia, uremic toxins, renin–aldosterone–angiotensin system, sympathetic nerve system, CKD-mineral bone disorder, malnutrition, inflammation, and oxidative stress, contribute to myocardial injury in patients with ESKD **(Fig. 1)**.

Furthermore, one of the contributors to myocardial injury in this population is believed to be coronary microcirculatory disturbance. Coronary flow reserve (CFR), an indicator of coronary microcirculation, is reported to decrease with declining glomerular filtration rate[3, 4], and most hemodialysis patients exhibit extremely low CFR. Additionally, it has been reported that reduced CFR is associated with mortality in hemodialysis patients[5]. Thus, impaired coronary microcirculation leads to myocardial injury through the reduction of myocardial oxygen supply. These pathophysiological mechanisms also involve intramyocardial arteriolar sclerosis and endothelial dysfunction, including reduced nitric oxide production. As anemia is reportedly related to the progression of left ventricular hypertrophy and fibrosis[6, 7], it may also contribute to the progression of myocardial injury due to reduced myocardial oxygen supply. Moreover, pathological findings indicate diffuse and patchy myocardial fibrosis in those with CKD, and it is particularly prominent around the intramyocardial arterioles[8]. A previous population-based autopsy study reported that reduced kidney function is associated with left ventricular hypertrophy and fibrosis[9], supporting these pathophysiological mechanisms.

Nakata, *et al* investigated the correlation between an imbalance in myocardial oxygen supply and demand and myocardial injury in a single-center cohort including 283 patients who had initiated hemodialysis[10]. In this study, hemoglobin levels were used as a surrogate marker of oxygen supply, and the rate pressure product was used as an indicator of oxygen demand. The findings revealed that the odds ratio for myocardial injury was significantly higher in the group with both increased oxygen demand and decreased oxygen supply compared to the well-balanced group.

Thus, in patients with CKD, especially ESKD, progression of anemia and vascular lesions is believed to be a crucial factor in the advancement of myocardial injury. Consequently, it is proposed that appropriate management of anemia, lipids, and blood pressure may arrest the progression of myocardial injury in this population. However, the target hemoglobin levels and treatment strategies that can improve coronary microcirculation remain unknown. Thus, further clinical and experimental studies are

Address for correspondence: Hideki Fujii, Division of Nephrology and Kidney Center, Kobe University Graduate School of Medicine, 7-5-2, Kusunoki-cho, Chuo-ku, Kobe, Hyogo 650-0017, Japan E-mail: fhideki@med.kobe-u.ac.jp

Received: January 4, 2024 Accepted for publication: January 9, 2024

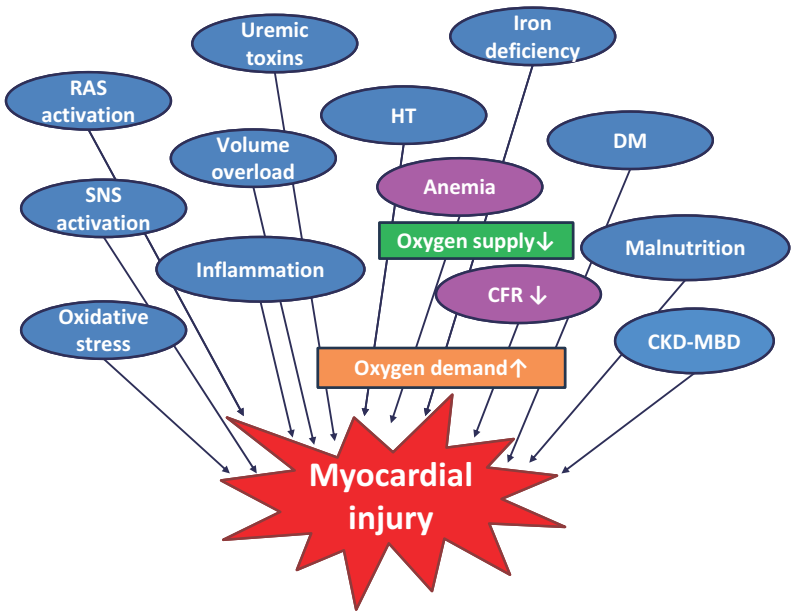

Fig. 1. Various factors contributing to progression of myocardial injury in patients with ESKD

ESKD, end stage kidney disease; RAS, renin–angiotensin–aldosterone system; SNS, sympathetic nerve system; HT, hypertension; CKD-MBD, chronic kidney disease-mineral bone disorder; DM, diabetes mellitus; CFR, coronary flow reserve.

required to address this issue. Moreover, the establishment of new treatments is anticipated in the near future to enhance the prognosis of patients with ESKD.

Conflicts of Interest

None.

References

1) Go AS, Chertow GM, Fan D, McCullough CE, Hsu CY. N Engl J Med, 2004; 351: 1296-1305
2) US Renal Data System 2022 Annual Data Report. Am J Kidney Dis, 2023; 81(3 Suppl1): A8-11
3) Fujii H, Takiuchi S, Kawano Y, Fukagawa M. Putative role of asymmetric dimethylarginine in microvascular disease of kidney and heart in hypertensive patients. Am J Hypertens, 2008; 21: 650-656
4) Charytan DM, Skali H, Shah NR, Veeranna V, Cheezum MK, Taqueti VR, Kato T, Bibbo CR, Hainer J, Dorbala S, Blankstein R, Di Carli MF. Coronary flow reserve is predictive of the risk of cardiovascular death regardless of chronic kidney disease stage. Kidney Int, 2018; 93: 501-509
5) Caliskan Y, Demirturk M, Ozkok A, Yelken B, Sakaci T, Oflaz H, Unsal A, Yildiz A. Coronary artery calcification and coronary flow velocity in haemodialysis patients. Nephrol Dial Transplant, 2010; 25: 2685-2690
6) Park SK, Jung JY, Kang JG, Hong HP, Oh CM. Association of Left Ventricular Hypertrophy with Hemoglobin Levels in Nonanemic and Anemic Populations. Cardiology, 2020; 145: 485-491
7) Niss O, Fleck R, Makue F, Alsaied T, Desai P, Towbin JA, Malik P, Taylor MD, Quinn CT. Association between diffuse myocardial fibrosis and diastolic dysfunction in sickle cell anemia. Blood, 2017; 130: 205-213
8) Tonelli M, Karumanchi SA, Thadhani R. Epidemiology and Mechanisms of Uremia-Related Cardiovascular Disease. Circulation, 2016; 133: 518-536
9) Izumaru K, Hata J, Nakano T, Nakashima Y, Nagata M, Fukuhara M, Oda Y, Kitazono T, Ninomiya T. Reduced Estimated GFR and Cardiac Remodeling: A Population-Based Autopsy Study. Am J Kidney Dis, 2019; 74: 373-381
10) Nakata K, Tanaka Y, Harada M, Hitaka M, Joki N. Association between Myocardial Oxygen Supply and Demand and Myocardial Injury in Patients with End-Stage Kidney Disease. J Atheroscler Thromb, 2024; 31: 540-549