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Reply: Letter to the editor

Pentosidine and soluble receptor for advanced glycation end-product (RAGE) are important prognostic factors independent of renal function in heart failure.

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We appreciate receiving a letter to the editor regarding our articles recently published in the Journal of Cardiac Failure (1, 2). In these articles, we have demonstrated that serum levels of pentosidine, one of well defined advanced glycation end-product (AGE), and soluble form of receptor for AGE (sRAGE) are novel markers to predict adverse clinical outcomes in patients with heart failure. Dr. Hartog et al. have pointed out the possibility that serum levels of AGE and sRAGE are affected by renal function. They have suggested to correct our data by estimated GFR calculated from the MDRD formula. It has been previously reported that accumulation of AGE including pentosidine increases with aging, in diabetes mellitus, and chronic renal failure with and without diabetes (3-6). Therefore, we excluded patients with renal insufficiency (creatinine > 2 mg/dl) in our studies. As Dr. Hartog et al. noted, eGFR from the MDRD formula is a prognostic factor in patients with chronic heart failure and systolic dysfunction. We have also reported the importance of renal function in heart failure (7). In our study subjects, serum levels of sRAGE, but not pentosidine, were negatively correlated with eGFR from the MDRD formula ($R = 0.42$, $P < 0.0001$), suggesting that sRAGE levels are affected by renal function (supplement data). Then, we re-analyzed our data adjusted for eGFR. As shown in Table, the multivariate Cox proportional hazard analysis revealed that sRAGE (hazard ratio 1.85, 95% confidence interval 1.13 – 3.04, $P = 0.014$) and pentosidine (hazard ratio 1.53, 95% confidence interval 1.07 – 2.17, $P = 0.018$) were independent prognostic factors when adjusted for eGFR. These data suggest that pentosidine and sRAGE are independent markers for risk stratification of patients with heart failure.

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Table. Results of the multivariate Cox proportional hazard analysis.

Variables	chi-square	HR	95% CI of HR	P value
Log (sRAGE) (per one SD increase)	5.99	1.85	1.13 – 3.04	0.014
Log (pentosidine) (per one SD increase)	5.58	1.53	1.07 – 2.17	0.018
Log (BNP) (per one SD increase)	2.39	1.63	0.88 – 3.03	0.122
eGFR (per one SD increase)	0.74	1.18	0.82 – 1.71	0.391
NYHA (class III / IV vs. class I / II)	0.28	1.31	0.49 – 3.52	0.598
EDV (per one SD increase)	0.25	1.11	0.75 – 1.66	0.619

BNP, B-type natriuretic peptide; eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association; EDV, left ventricular end-diastolic volume.

HR, hazard ratio; CI, confidence interval

Figure. 1



