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Midterm measurement of cystatin C predicts preeclampsia

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Objectives : Underlying renal function has been strongly associated with pregnancy prognosis. Several small reports demonstrated that serum level of cystatin C, one of the novel marker for kidney function estimation, was increased in those who experienced preeclampsia. However, the predictive value of cystatin C level for preeclampsia was yet to be examined prospectively in general mothers.

Methods : We prospectively measured serum cystatin C and creatinine level of singleton pregnant women without severe comorbidity in their midterm, during gestational age from 22 weeks to 30 weeks, in two tertiary hospitals in Korea. Mothers were enrolled to the study between October, 2014 and September, 2016. The study outcome was events of preeclampsia, diagnosed by attending obstetrician from clinical findings of hypertension, proteinuria, and evidence of end-organ damage. We first compared the median level of renal function parameters by Mann-Whitney U test between those who were preeclamptic and not. In addition, we constructed receiver operating characteristic (ROC) curve with the parameters as an explanatory variable and calculated the area under curve (AUC). We also investigated whether levels of renal function parameters were associated with increased risk of preeclampsia by multivariable logistic regression test.

Results : There were 688 mothers initially enrolled for the study with informed consent. After excluding those with follow-up loss (n=60) and did not measured midterm cystatin C level (n=48), 580 mothers were included in the final study cohort. The median age was 32 (29-34) years old, and only two mothers had previous history of hypertension. There were 8 (1.3 %) mothers who consequently experienced preeclampsia. The median cystatin C level was significantly different between those who experienced preeclampsia [0.800 (0.720-0.958)] and those who did not [0.722 (0.660-0.792) (P=0.027), although co-measured creatinine (P=0.217) level did not show meaningful difference. The calculated AUC of the ROC curve of cystatin C for prediction of

preeclampsia event was significant higher than the AUC of ROC when using creatinine as an explanatory variable (0.7279 .vs 0.4974, P=0.003). Moreover, when adjusted for age and multiparity, the increment of cystatin C value for 0.1 mg/dL was significantly associated with increased risk of preeclampsia (adjusted OR 1.608, 95% CI 1.021-2.534, P=0.040) when creatinine level did not show relevant relationship with the risk of preeclampsia events (adjusted OR 0.865, 95% CI 0.408-1.835, P=0.706)

Conclusions : Measuring cystatin C level had benefit in terms of predicting preeclampsia despite its low incidence in general mothers without severe comorbidities, and its predictive value was significantly better than that of serum creatinine. Therefore, clinicians should consider routine measurement of cystatin C during midterm.

Keywords : Preeclampsia, Cystatin C, Pregnancy, Creatinine