

Could YKL-40 be used as a new marker for coronary artery ectasia?

YKL-40 kullanımı koroner arter ektazi için yeni bir belirteç olabilir mi?

Coronary artery ectasia (CAE) is defined as localized or diffuse dilatation of the coronary lumen that exceeds the diameter of normal adjacent segments or the diameter of the patient's largest coronary artery by 1.5 times (1), and has various classifications according to the size of luminal diameter, geometry, and the presence of vascular layer. Since the prevalence of CAE is relatively rare (0.2-10%) and the nature history of CAE is unknown yet (2), the clinical impact of CAE tends to overlook in real practice. Although the pathogenic mechanisms of CAE are not fully known, it has been suggested that CAE is linked to coronary atherosclerosis in terms of histopathologic aspects (1, 2). The basic pathobiologic process in CAE has been associated with enzymatic degradation of the extracellular matrix (ECM) of the media, especially overexpression of matrix metalloproteinases (MMPs), which could result in excessive expansive arterial remodeling (2, 3). Previous studies have reported that various factors can affect the development of coronary ectasia, which are either directly or indirectly related to the atherosclerotic evolution (2). In particular, inflammation plays a key role in the development of coronary artery ectasia. Several studies have revealed that levels of adhesion molecules, C-reactive protein, and vascular endothelial growth factor were higher in patients with coronary artery ectasia (2, 4).

YKL-40, a new biomarker of inflammation, is secreted by activated macrophages and neutrophils in different tissues with inflammation (5, 6). Although the definite function of YKL-40 is not completely established yet, it has been demonstrated that YKL-40 induces the maturation of monocytes to macrophages at early stage of atherosclerosis. This action henceforth could contribute to a series of process that inflammatory mediators from activated macrophages promote vascular smooth muscle cell (VSMC) migration and proliferation, and ECM degradation may cause the formation of coronary ectasia via arterial remodeling (7).

Erdoğan et al. (8) report in the Anatolian Journal of Cardiology that serum YKL-40 levels in patients with isolated CAE and coronary artery disease are significantly higher than that in patients with normal coronary artery (NCA) and this result in those with isolated CAE remains significant even after adjusting for multiple variables. Furthermore, the present study demonstrates that

C-reactive protein (CRP) level in between those with isolated CAE and NCA does not have a significant difference, which is different from the previous study (4). As a conclusion, the authors mention that this study is a first study showing high serum YKL-40 levels independent of increased systemic inflammatory response in patients with isolated CAE. Considering previous studies about pathogenic mechanisms in the formation of coronary ectasia, this study suggests the possibility of the relation of YKL-40 on the development of CAE. However, important details in assessing the association between YKL-40 and isolated CAE in this study are not provided. There is no clear description about whether this study is retrospectively or prospectively designed, how many patients have isolated CAE among the entire population, and which method was used for matching the groups. Thus, this study has selection bias. The present study also has some issues with respect to statistical analyses. This study compares YKL-40 level among the three groups (NCA, isolated CAE, and CAD) in the design of the study. However, logistic regression analysis in Table 2 (doi: 145) presenting the main result shows comparison between the two groups (NCA versus CAE). This analytic method seems not to be right and p value in this analysis would be significant when p value is <0.0025. The multinomial regression analysis among the three groups would be needed. In addition, CRP and YKL-40 levels in this study show wide distribution. For the statistical analyses, nonparametric tests or transformations of the values for normal distribution would be necessary.

Previous studies have reported that circulating YKL-40 level is elevated in patients with diabetes and obesity (7-10). The entire population in the present study has high body mass index, and the prevalence of diabetes in patients with CAE and CAD tends to be higher than in those with NCA, although there is no significant difference between the groups. Accordingly, increased YKL-40 level in patients with CAE and CAD might not be explained only by these conditions themselves.

With respect to YKL-40 linked to ischemic heart disease such as acute coronary syndrome and stable angina, most of previous studies have reported relevant results that YKL-40 levels are higher in patients with acute myocardial infarction than the controls and elevated YKL-40 level in patients with stable coro-

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nary artery disease is an independent predictor of overall and cardiovascular mortality (11, 12). Although there is no regression analysis of the association of YKL-40 with CAD group compared to NCA group and no information on clinical presentation of the CAD group in the authors' study, it would be presumed to be the relation of YKL-40 with CAD from the result in Figure 1.

The authors' study can be meaningful as a first study demonstrating a probability of the involvement of YKL-40 on the development of CAE. There are still many unanswered questions. Normal range for circulating YKL-40 in healthy population is not fully established. Will YKL-40 be a key factor but not one of inflammatory factors involved in coronary ectatic change? YKL-40 requires more indisputable evidences to play a role as a biomarker in coronary artery ectasia, although circulating YKL-40 may reflect coronary atherosclerotic process and could be a prognostic marker in patients with ischemic heart disease. Experimental researches also would be necessary to define the molecular mechanisms related to coronary ectasia. In addition, further longitudinal studies are needed to assess whether change of YKL-40 level influences change of coronary atherosclerotic burden, and can predict clinical outcome.

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