

## Periostin-binding DNA aptamer ameliorates peritoneal dialysis-induced peritoneal fibrosis

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**Background:** Peritoneal fibrosis (PF) is a major complication in patients on peritoneal dialysis (PD). In PD-related PF, the protein expressions of various extracellular matrix including periostin are known to be increased via the transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1) pathway. This study was undertaken to evaluate the impact of periostin inhibition by novel aptamer-based inhibitor on TGF- $\beta$ 1-induced epithelial-mesenchymal transition (EMT). **Methods:** In vitro, primary HPMCs were exposed to TGF- $\beta$ 1 (2 ng/ml) to induce EMT and fibrosis with or without periostin siRNA (100 nM) or periostin-binding DNA aptamer (200 nM). In vivo, PD catheters were inserted into 48 C57BL/6 mice, and saline (C group, N=24) or 4.25% PD solution (PD group, N=24) was infused for 4 weeks. Twelve mice from each group were treated with periostin-binding DNA aptamer (500  $\mu$ g/kg/d) (PA). mRNA and protein expressions of periostin, fibronectin,  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA), snail, and E-cadherin in HPMCs and mouse peritoneum were evaluated by quantitative real-time polymerase chain reaction and western blot analysis, respectively. PF was also assessed by Masson's trichrome (MT) staining. **Results:** In vitro, TGF- $\beta$ 1 treatment significantly up-regulated periostin, fibronectin,  $\alpha$ -SMA, and snail expressions, while E-cadherin expression was significantly decreased by TGF- $\beta$ 1 in cultured HPMCs ( $p < 0.01$ ). Not only periostin siRNA but also periostin-binding DNA aptamer significantly attenuated TGF- $\beta$ 1-induced periostin, fibronectin,  $\alpha$ -SMA, and snail expressions and significantly restored E-cadherin expression in HPMCs ( $p < 0.05$ ). In vivo, the expressions of periostin, fibronectin,  $\alpha$ -SMA, and snail were significantly increased, whereas E-cadherin expression was significantly decreased in the peritoneum of PD mice ( $p < 0.05$ ). The thickness of the submesothelial layer and the intensity of MT staining in the peritoneum were significantly higher in PD mice compared to C mice ( $p < 0.05$ ). These changes in the PD group were significantly abrogated by PA treatment ( $p < 0.05$ ). **Conclusions:** These findings suggest that PA can be a potential therapeutic strategy for PF in PD patients.

## Subclinical Liver Stiffness is Closely Related with Albuminuria in Healthy Subjects

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**Objective:** Recent evidences demonstrated that liver has a pivotal role in metabolic derangement, and adipokines and cytokines interplay with liver injury including hepatic steatosis and fibrosis. We investigated that the association between subclinical liver stiffness (LS) measured by transient elastography and UACR in healthy individuals. **Design and Method:** The study population was all subjects who underwent transient elastography at Yonsei University Health System between November 2011 and June 2015. Among 4,236 patients, we excluded 3,508 individuals who have recognized with underlying liver disease, decreased renal function. 582 subjects were eligible for the present analysis after propensity score matching. Multiple logistic regression was performed to elucidate the association between LS and UACR in propensity score matched individuals. **Results:** The mean age was 60.8 $\pm$ 13.6 years, 369 (63.4%) patients were male. The median UACR was 15.4 (6.9-79.7) mg/g Cr, the median value of LS was 4.7 (4.0-5.8) kPa. The subjects were divided into two groups according to the median value of log LS levels. After matched for age, gender, history of hypertension, diabetes, and eGFR, low LS group showed significantly lower levels of fasting plasma glucose (110.4 $\pm$ 34.3 vs. 119.9 $\pm$ 49.1 mg/dL,  $p = 0.007$ ), AST (20 [17-25] vs. 23 [18-31] U/L,  $p < 0.001$ ), ALT (18 [13-25] vs. 20 [15-30] U/L,  $p = 0.002$ ), hs-CRP (0.80 [0.50-2.00] vs. 1.50 [0.70-6.95] mg/L,  $p < 0.001$ ), and UACR (13.1 [6.3-55.8] vs. 18.4 [8.1-130.0] mg/g Cr,  $p = 0.014$ ), while total cholesterol (174.8 $\pm$ 39.3 vs. 166.0 $\pm$ 46.9 mg/dL,  $p = 0.015$ ) and serum albumin (4.2 $\pm$ 0.4 vs. 3.9 $\pm$ 0.6 mg/dL,  $p < 0.001$ ) showed significantly higher levels in low LS group compared with high LS group. In multiple logistic analysis, LS was significantly associated with the presence of microalbuminuria (UACR  $> 30$  mg/g Cr in a crude model (LS, 1log increase, odds ratio [OR] = 2.114, confidence interval [CI] = 1.444-3.096,  $p < 0.001$ ). **Conclusions:** Present study showed that the subclinical LS was significantly associated with the presence of microalbuminuria even in relatively healthy subjects. This finding may provide an evidence that liver dysfunction correlates with kidney injury represented by microalbuminuria.