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授与した学位	博士
専攻分野の名称	医学
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学位授与の要件	医歯薬学総合研究科社会環境生命科学専攻 (学位規則第4条第1項該当)
学位論文題目	C-reactive protein is associated with cigarette smoking-induced hyperfiltration and proteinuria in an apparently healthy population (健診受診者においてC反応性蛋白は喫煙に起因する糸球体過剰濾過と高度尿蛋白に関連する)
論文審査委員	教授 土居 弘幸 教授 公文 裕巳 准教授 和田 淳

学位論文内容の要旨

Although cigarette smoking is known to be an important risk factor for renal disease, the mechanism by which smoking induces progressive renal disease in a healthy population has not been established. We hypothesized that oxidative stress (measured as 8-iso-prostaglandin F_{2α}, 8-iso-PGF2a), inflammation (highly sensitive C-reactive protein (CRP), hs-CRP) and nitric oxide may be associated with an alteration in the estimated glomerular filtration rate (eGFR) and proteinuria in otherwise healthy smokers. A total of 649 eligible subjects were classified according to their smoking status. Plasma NOx was measured using ozone-based chemiluminescence, urinary 8-iso-PGF2a was measured using enzyme immunoassay and serum hs-CRP was measured using a latex aggregation nephelometry method. The levels of 8-iso-PGF2a and hs-CRP increased in current smokers ($P=0.001$ and $P=0.029$, respectively), although there was not an increase in the NOx level. The prevalence of a high eGFR increased in light smokers (odds ratio (OR) 1.15 (95% confidence interval (CI), 0.61–2.17)) and heavy smokers (OR 2.33 (95% CI, 1.06–5.10)) when compared with non- and past smokers (P for trend=0.024). The multivariable-adjusted mean values of the eGFR in current smokers, reported from the lowest to the highest quintiles of hs-CRP levels, were 82.1, 85.1, 86.4 and 88.5 ml per min per 1.73m² (P for trend=0.027). The mean values of proteinuria were 28.6, 34.6, 37.2 and 39.5 mg/g creatinine (P for trend=0.003). The correlation coefficient between hs-CRP and eGFR was increased significantly ($P=0.03$) across non- ($r=0.03$), past ($r=-0.17$), light ($r=0.13$) and heavy smokers ($r=0.31$). In conclusion, cigarette smoking is a risk factor for renal function alteration in healthy smokers and is characterized by a high eGFR and a high urinary protein associated with an increase in the hs-CRP. This finding suggests that hs-CRP may help mediate the alteration of renal function in smokers.

論文審査結果の要旨

健康人を対象とした、喫煙を曝露とした腎血流量の変化を評価したものである。

対象が健康人であること、クロスセクショナルスタディであることが、上記の因果関係を明らかにするには、本研究の限界となっている。

しかしながら、検査方法の精度、データ分析、そしてその考察能力は、今後の研究の発展性に大きな期待が持てる。

よって、本研究者は博士（医学）の学位を得る資格があると認める。