

Reduced Renal Function and Stroke Subtypes

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Although some studies have shown that reduced renal function was associated with increased risk of ischemic stroke but not hemorrhagic stroke^{1,2}, there are other studies that reported the positive association between reduced renal function and hemorrhagic stroke^{3,4}. To explain the reason of those inconsistent results, the mechanism underlying the association between reduced renal function and incidence of stroke should be taken into consideration.

The potential mechanism that underlies between reduced renal function and incidence of stroke is shown in **Fig. 1**. Endothelial injury is the initial process leading to glomerular dysfunction (reduced renal function) and atherosclerosis⁵. However, the progression of atherosclerosis is also a result of aggressive endothelial repair, and reduced renal function is a result of inappropriate endothelial repair. Because the aggressive stage of endothelial repair is closely associated with the deficient stage of endothelial repair⁶ that induces endothelial dysfunction and glomerular dysfunction, atherosclerosis could be associated with reduced renal function. Aneurysm, which is a known cause of subarachnoid hemorrhage (SAH), is also associated with endothelial dysfunction. Therefore, reduced renal function could be positively associated with atherosclerosis-related cerebral infarction and SAH. In addition to that, because endothelial repair has beneficial influence on the maintenance of microcirculation by stimulating angiogenesis and maturation of immature vessel⁷, inappropriate endothelial repair could disrupt microcirculation that is associated with arteriosclerosis and hypertension. In this way, reduced renal function could be associated with arteriosclerosis (small artery)-related stroke, such as lacunar infarction and intracerebral hemorrhage. Furthermore, because platelet also takes an important

role in endothelial repair⁶, thrombosis could be induced in the process of endothelial repair. Therefore, reduced renal function can be associated with all types of stroke. Because endothelial injury is the initial process of the aforementioned mechanisms, the magnitude of endothelial injury could determine the strength of the association between reduced renal function and stroke and where in the process of endothelial repair might determine which type of stroke would be associated with reduced renal function. Therefore, the factor that influenced the activity of endothelial repair could act as a determinant of the association between the subtype of stroke and reduced renal function³.

In this issue of the journal, independent from known cardiovascular risk factors, Oh *et al.* found that reduced glomerular filtration rate (GFR) < 45 mL/min/1.73 m² was associated with increased risk of ischemic stroke in Korean men but not in Korean women⁸. Because Korean men have higher rates of smoking, alcohol intake, and hypertension than Korean women⁹, the association between reduced renal function and ischemic stroke could be stronger for men than that for women. In addition to that, in this study, by use of the crude model, with the reference group of GFR ≥ 90 mL/min/min, men with GFR 45–59 mL/min/1.73 m² and women with GFR 30–44 mL/min/1.73 m² showed significantly higher risk of hemorrhagic stroke. However, after adjusting for age, those significant associations disappeared. Because aging is associated with increased risk of endothelial injury and reduced activity of endothelial repair⁶, aging could influence both reduced renal function and hemorrhagic stroke by disrupting microcirculation. In other words, age-related disruption of microcirculation could cause both hemorrhagic stroke and reduced renal function. Taken together, reduced renal function could act as an indicator of age-related disruption of microcirculation, which is a known risk for hemorrhagic stroke.

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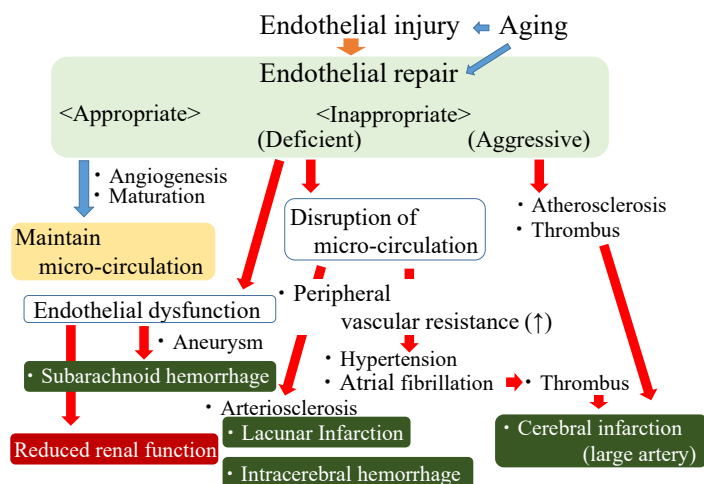


Fig. 1. Potential mechanism underlying the association between reduced renal function and incidence of stroke

Disruption of microcirculation might also cause arteriosclerosis-related infarction known as lacunar infarction. In this study, after adjusting for age, the positive association shown between reduced renal function and ischemic stroke became weak in men and disappeared in women. Because the subtypes of ischemic stroke were not determined in this study, the influence of age-related disruption of microcirculation on the association between reduced renal function and stroke could not be discussed in their study regardless of the fact that the most common type of stroke in South Korea was large artery atherosclerosis¹⁰⁾. Therefore, in this study, the age-adjusted model might have enhanced the influence of reduced renal function on large artery atherosclerosis and reduced its influence on microcirculation disruption.

In summary, the study by Oh *et al.* showed that, independent from known cardiovascular risk factors, reduced GFR <math>< 45 \text{ mL/min/1.73 m}^2</math> was associated with an increased risk of ischemic stroke only for men. This finding is clearly important for risk estimation of stroke for participants with reduced renal function. Furthermore, this study also showed that the influence of age on the associations between reduced renal function and (both for ischemic and hemorrhagic) stroke is strong. These findings might also be informative knowledge to clarify the mechanism underlying the association between reduced renal function and stroke subtypes.

Conflicts of Interest

None.

Reference

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