



## The relationship between renal artery stenosis and ischemic nephropathy

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### ABSTRACT

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Ischemic nephropathy is defined as a clinically significant progressive reduction in glomerular filtration rate that is usually associated with significant renal artery stenosis (unilateral or bilateral involvement). Atherosclerotic renal artery disease is known as the most common cause of the ischemic nephropathy. These patients may develop secondary hypertension. In addition, epidemiologic data has showed a clear association between atherosclerotic renal artery stenosis and coronary artery disease and other cardiovascular disease. Despite the preserving function of kidney on various autoregulation processes, unusual microvascular function will be resulted due to sustained decline in renal perfusion. The ischemic nephropathy of asymptomatic cases may result in renovascular hypertension and renal failure. The reduction of renal function in these patients might be decreased or stopped by early appropriate diagnosis and also might be treated with renal artery angioplasty or surgery, after medical management. There is a debate about the occurrence of ischemic nephropathy as a result of atherosclerotic renal artery stenosis. In this study we aimed to review the prevalence of ischemic nephropathy due to atherosclerotic renal artery stenosis.

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### Introduction

The ischemic nephropathy is a disease which can be reflected through occlusive

disease of the main renal arteries and finally can lead to the chronic renal failure.

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Atherosclerotic renovascular disease (ARVD) can result in renovascular hypertension. ARVD is known as an aging associated disease. Several studies have shown its strong correlation with extrarenal atherosclerotic disease (1,2). ARVD is a great risk factor of the cardiovascular death than renal replacement therapy (3). The efficacy of renal revascularization on the renal and cardiovascular output has not been approved certainly (4).

Diagnosis and reversing the sustained decrease of kidney function due to occlusive disease of the renal arteries have become one of the major clinical challenges. Renal artery stenosis has shown considerable association with declining in kidney function, accelerated cardiovascular disease, and increased mortality and morbidity. Despite medical therapy for controlling the cardiovascular diseases, renovascular hypertension can result in refractory hypertension, tubulointerstitial fibrosis, heart and renal defects (5).

Improvement of imaging techniques and devices has been beneficial in controlling the declining of the kidney function. Surgical revascularization or percutaneous transluminal renal angioplasty can treat the ischemic nephropathy which reduce or delay the risk of the occurrence or progress of chronic renal disease. In this regard the early diagnosis of the ischemic renal disease should be noticed (6).

According to previous studies, revascularization leads to the increases of the glomerular filtration of some patients with defected renal function (almost 25 to 30%). Other patients with impaired renal function have shown no improvements in renal function or even loss of the kidney function. Due to the recovery of cases with defected renal function after the renal revascularization, the large-vessel occlusive disease might be proposed as a great risk

factor of the renal dysfunction (5).

The mentioned concept about the effect of renal artery disease in renal defects has been studied since 1980s (5,7). The treatment of renal function after the revascularization might reduce the requirement of further therapies such as dialysis. Atherosclerotic renal artery stenosis (RAS) mostly appears asymptomatic which difficult the early diagnosis of the diseases. Therefore the prevalence of the disease could not be estimated exactly (6).

### ***Epidemiology and prevalence***

According to the previous estimations the atherosclerosis accounts for almost 90% of the adults with RAS (4,5). Based on some reports, the RAS has been observed in 38% of the patients with aortic aneurysm, 33% of patients with aortic occlusive disease, and 39% of those with lower limb occlusive disease (4,8). In one study the renal angiography was used as a diagnostic procedure for patients with severe hypertension, chronic kidney disease, and acute pulmonary edema with hypertension or atherosclerosis. According to this study the AVR and RAS were detected in 39% and 14% of the studied patients (9). In another study the AVR and RAS were present in patients with congestive heart failure and they showed higher creatinine levels and peripheral vascular disease (3). 5 to 8% of cases with ESRD have also showed the presence of RAS (10). Coronary artery disease (CAD), peripheral vascular disease, diabetes, dyslipidemia, or hypertension (HTN) are mentioned in different studies as various risk factors of the RAS (11).

Various conditions of the patients such as age, smoking, hypertension, dyslipidemias, and diabetes are proposed as different parameters that increase the risk of aortic atherosclerotic plaques occurrence (12).

The prevalence of the chronic renal

diseases such as ESRD, due to renovascular diseases, is not clear (5).

The decline of kidney function which is correlated to ischemic nephropathy has been observed in patients with renal artery disease of the entire renal mass. Reduction in GFR for cases with unilateral renovascular disease has been rarely improved after renal revascularization (13).

According to the previous assessments the real incidence of ischemic nephropathy as a cause of end-stage renal has increased in past years (14). An intense correlation has been also identified between atherosclerotic renal-artery stenosis (ARAS) and cardiovascular impairments through epidemiologic surveys. The improvements of the antihypertensive pharmacotherapy and intensive control of the risk factors including smoking, cessation, and statin therapy might lead to excellent blood pressure control of various cases (15).

### **Pathogenesis**

The situations which lead to ischemic nephropathy appear to be more complex than narrowing of the renal artery due to atherosclerotic RAS (16).

Because of the metabolic requirements of the kidney, the reduction of renal blood flow (RBF) in the presence of anatomic lesions may not be enough for the reduced renal function (4,17).

Autoregulation can support the physiological processes during reductions in renal perfusion pressure and GFR (18). Lack of red cell and oxygen delivery due to diminished kidney blood supply cannot induce the atrophy and fibrosis in cases with atherosclerotic RAS.

Studies of the Doppler ultrasound renal resistive index, revealed that high parenchymal resistance predicts weak renal functional recovery after revascularization (5,19). Individual case reports demonstrated that even intense renal impairment might be

reversed, particularly when capsular blood vessels are maintained (5).

### **Clinical presentation**

Based on various surveys, the ischemic nephropathy caused by RAS might be illustrated through different clinical syndromes including progressive azotemia, acute renal failure induced by angiotensin-converting enzyme inhibitor (ACEI), flash pulmonary edema, proteinuria (nephrotic-range proteinuria), etc. (4,6,14).

Proteinuria which influence through increasing the intrarenal level of Ang II, was proposed as a criterion of severity of parenchymal disorder in atherosclerotic nephropathy for patients with RAS (4,20,21).

### **Diagnosis**

Due to the importance of the early diagnosis of patients with the ischemic nephropathy several examination have been recommended for considering the kidney function, size, vascular anatomy, and the presence of the atherosclerotic renovascular lesions. The intervention of the atherosclerotic plaques in decreasing the GFR should be assessed through additional tests (4,22).

Conventional angiography, spiral computed tomography (CT) angiography, and magnetic resonance angiogram (MRA) are the most frequent used techniques which would demonstrate the abnormal conditions of renal arteries. Performing renal-vein-renin measurement, ACEI renography, and color Doppler sonography have been suggested to identify any impairment of renal functions caused by RAS. For evaluating the extent of the vascular stenosis, duplex Doppler ultrasonography has been used which provide data about the intrarenal resistive index.

ACEI renography is another effective screening procedure which can be applied for patients with RAS that have normal renal function.

### **Treatment**

Although various researches have been conducted on the controlling ischemic nephropathy, there is still great controversy about the benefits of revascularization and appropriate management of the RAS in these patients (4). There are different comorbidities along with the ischemic nephropathy which complicate providing the comprehensive data about the efficacy of the revascularization including coronary artery disease, congestive heart failure, cerebrovascular accident, chronic kidney disease, diabetes, etc. (23). There are no randomized control trial which confirm the concept that revascularization inhibits the progression of the chronic kidney disease.

One trial which compared the efficacy of medical treatment with the angioplasty in recovering the patients with AVR resulted in little advantage of the angioplasty over pharmacotherapy in the treatment of the AVR (24,25).

According to the previous studies, medical management would be the primary choice for treating the renovascular hypertension. In the majority of the patients who have undergone different interventions the progression of the vascular stenosis has been inhibited but they have showed little or any improvement in their kidney function. Some patients develop more progressive decline in their renal function early after the revascularization technique (mostly patients under surgery, angioplasty or stenting).

Several meta-analyses resulted in suitable blood pressure control and renal function enhancement with percutaneous transluminal renal angiography plus stent compared with conventional medical therapy (14).

### **Conclusion**

Ischemic nephropathy is a common age dependent disease which could be caused due to lesions of atherosclerotic

renovascular disease and renal artery stenosis. Despite various examinations regarding the renal revascularization of patients with renal diseases, only few prospective randomized trials have been conducted which did not obtain benefits either with endovascular stents or with surgery, addition to the effective medical therapy. Meaningful enhancement of kidney function after revascularization is limited in patients. The early diagnosis of patients at risk of chronic kidney disease and those which benefit from different interventions is the main purpose of the researchers in this medical field which should be addressed in future trials.

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### **Conflict of Interest**

The authors declare no conflict of interest.

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