Review Article

Endovascular Intervention for Renal Artery Stenosis in Renal Transplant

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Renal artery stenosis occurs in 1% to 16% of adult renal transplant recipients. Revascularization improves renal function and leads to better blood pressure control. Angioplasty is usually attempted first. A vascular stent is used if there are complications with angioplasty or if there is recurrent stenosis after repeated angioplasty. Complications of angioplasty or stent insertion, though rare, may have severe consequences and lead to graft loss. In-stent restenosis is a major concern with the use of vascular stents. [*Hong Kong J Nephrol* 2003;5(2): 73–7]

Key words: kidney transplantation, renal artery stenosis, angioplasty, stents, complications

在腎臟移植接受者中，術後腎動脈狹窄的發生率約在1-16%之間。對於這類病人，血管的再疏通 (revascularization) 可帶來腎功能的改善，並有助於血壓的控制。一般建議，血管成型術 (angioplasty) 是首先的選擇；血管支架 (stent) 的植入，則通常保留給出現併發症的血管成型術接受者、或在重複的血管成型術後出現再狹窄的病人。血管成型術或支架植入術的併發症雖然罕見，但卻可能會造成嚴重的後果甚至植入腎臟的喪失。另外，在血管支架的植入術中，支架內發生的再狹窄亦是一個備受關注的問題。

Introduction

Renal artery stenosis (RAS) occurs in 1% to 16% of adults after renal transplant, depending on the diagnostic criteria used and indications for arteriography [1–7]. The interval between transplantation and diagnosis of transplant RAS ranges from 2 to 45 months (range of mean, 10–21 months) [6]. Different etiologic factors have been postulated, including faulty surgical technique, postoperative periarterial fibrosis, immune response, cytomegalovirus infection, long cold ischemia time, atherosclerosis, trauma, and chronic rejection [4,7–16]. The etiologies are mostly different from those causing RAS in native kidneys.

RAS is important in renal transplant because it occurs in a solitary kidney, which is precious to the patient. Prolonged RAS may cause renal ischemia, leading to hypertension and uremia. Revascularization will improve renal function and lead to better blood pressure control [8,17]. RAS should be suspected if there is worsening renal function, problems with blood pressure control, or progressive deterioration in these parameters. Non-invasive imaging methods should be used to confirm or exclude the diagnosis. The most commonly used modality is ultrasound with Doppler study. Contrast-enhanced magnetic resonance angiography (CE-MRA) and computed tomography angiography (CTA) are usually used to confirm RAS diagnosed by Doppler ultrasound. CE-MRA and CTA can produce three-dimensional images that provide information on the orientation of the arteries, which is important in choosing the correct plane of projection during subsequent intervention.

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Treatment Options

Even when RAS is diagnosed, not all patients will immediately undergo angioplasty or surgery. RAS can be managed with antihypertensive drugs. The risk of vascular injury and loss of the graft kidney during angioplasty or surgery must be balanced against the benefit of revascularization. There is no hard and fast rule in this, but the severity of impairment, difficulty in blood pressure control, and rapidity of worsening function may provide the best indications for intervention.

One may choose either surgical means or endovascular means of revascularization. There is no randomized control trial comparing the results of endovascular intervention and surgery. Each method has its own advocates. Surgery was favored in the late 1980s and early 1990s, when one study showed that the immediate success rate with surgical repair (SR) was 92.1%, compared with 69% with percutaneous transluminal angioplasty (PTA) [18]. The long-term success rate was 81.5% with SR and 40.8% with PTA, with a mean follow-up period of 56.7 months and 32 months, respectively. It is outside the scope of this paper to discuss techniques of surgical revascularization. Most practitioners will choose endovascular means as the first line of intervention due to its technical effectiveness and better tolerance by patients. It also does not preclude subsequent surgical correction if required.

RAS can occur in different anatomic locations. It is mostly seen in the arterial anastomosis between the graft renal artery and the recipient artery. It may also be seen along the main renal artery or in the intrarenal branches. Occasionally, arterial stenosis is present in the external iliac artery or internal iliac artery of the recipient, which may produce similar clinical pictures. Another variant is vascular kinking.

Procedure

Anastomotic strictures and strictures in the main renal artery may be treated using balloon angioplasty supplemented with vascular stenting, if necessary. Intrarenal stricture may need to be treated according to the etiology, since graft rejection may produce multiple strictures in the intrarenal branches, and the clinical course may not be changed by PTA. Stenosis in the iliac arteries may be treated using angioplasty or stenting, but one should be careful not to occlude the orifice of the renal artery if the graft is anastomosed to the external iliac artery and the stricture is just adjacent to the anastomosis. Functionally significant vascular kinking is better treated by surgical means [19].

The stricture is often approached from the common femoral artery. If the anastomosis is in the internal iliac artery, one usually approaches from the contralateral femoral artery. If the anastomosis is in the external iliac artery, one may approach from either the ipsilateral or contralateral femoral artery, depending on the configuration of the anastomosis. The stenosis is confirmed through a femoral arterial sheath and diagnostic catheter. Non-ionic contrast medium is now used routinely to minimize contrast nephrotoxicity. If the patient has severely impaired renal function, a dimer contrast agent may be used, as it is iso-osmolar with blood and is, theoretically, less nephrotoxic [20,21]. Recently, carbon dioxide- and gadolinium-based contrast have been used for angiography (Figure 1). Carbon dioxide provides negative contrast and gadolinium-based agents are primarily used in magnetic resonance imaging. Both types of contrast media are much less nephrotoxic than iodine-based contrast, but the contrast resolution is not as good [22–27].

Before angioplasty, we give at least 5,000 units of heparin for systemic anticoagulation; 0.2 mg intra-arterial nitroglycerin is also given to the distal renal branch to prevent arterial spasm. The stenosis is traversed with a guidewire and a balloon catheter is used to dilate the stricture. The diameter of the balloon used is about 10% larger than the diameter of the artery, which is measured using calibration software in the angiography equipment. The intra-arterial pressure gradient across the stricture is measured after angioplasty. If the residual stenosis is less than 30%, or the pressure gradient across the stricture is less than 15 mmHg, we may stop and follow up the patient (Figure 2). If both parameters are unsatisfactory, one may consider implantation of a renal stent.

A renal stent is also indicated if there are angioplasty complications, such as arterial dissection, or if there is recurrent stenosis after repeated angioplasty. For renal stenting, a balloon-expandable stent is usually used. A very short stent can be deployed in this way and the placement is precise. The newer generation of stents have a lower profile and cross the curves and angles quite readily with the use of a guiding catheter. The stent is deployed across the stricture under continual angiographic guidance, and the final result is confirmed using angiography. A stent will usually produce an immediate satisfactory result. If stricture is due to very resistant fibrosis, the stent may be compressed by the elastic force and the vascular lumen will not be fully opened.

Complications

Immediate complications of PTA are uncommon, and include arterial dissection, rupture, guidewire-induced vasospasm, and graft loss. A dissection may be treated with a renal stent; however, if the dissection is

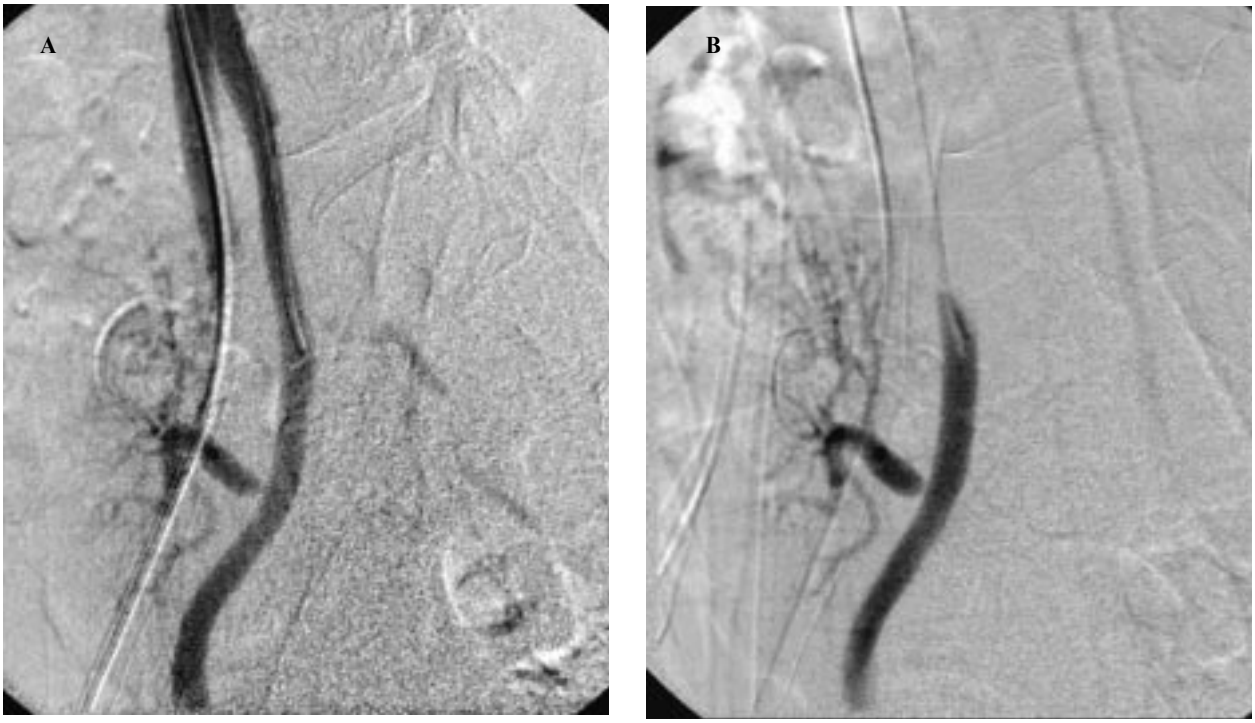

Figure 1. Carbon dioxide angiography (A) can provide similar information to iodinated contrast angiography (B), except that there is more noise in the carbon dioxide angiogram, which is due to the lower contrast resolution.

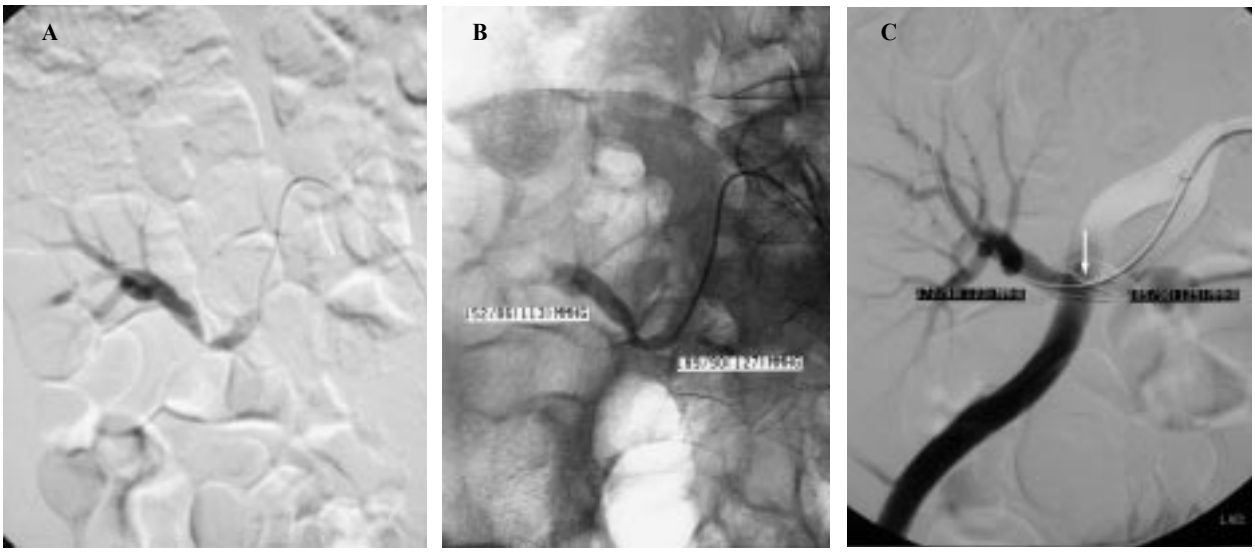

Figure 2. A tight renal artery stenosis (A) dilated with a 6 mm balloon, resulting in residual stenosis and a systolic pressure gradient of 37 mmHg (B). Even with implantation of a 6 mm metallic stent, the stricture is not fully expanded (arrow), probably due to periarterial fibrosis. The systolic pressure gradient becomes 13 mmHg, and the clinical response is satisfactory (C).

extensive, the graft may not be salvageable. A covered stent may be used for arterial rupture. In severe hemorrhage, emergency surgery may be necessary to salvage the kidney. Guidewire-induced spasm is usually relieved after the guidewire is withdrawn. If it is not, renal ischemia may have occurred due to unperfused renal parenchyma. Death related to the procedure has been reported, although it is rare. Other remote complications, such as postoperative myocardial infarction and complications related to the use of

heparin, are possible [28]. Early postoperative complications of angioplasty and stent implantation include the risk of early arterial thrombosis. Therefore, oral aspirin for at least 6 months and clopidogrel for 1 month are recommended. Cholesterol embolization is less likely after PTA and stenting in the renal graft since the etiology of the stricture is different from that of RAS in native kidneys. The major late complication of PTA is restenosis, which usually appears 6 to 8 months after angioplasty [13], and which is usually the result of intimal hyperplasia. In-stent restenosis also occurs after stent placement.

Outcome

Though there are many medical reports that discuss this topic, nearly all are limited by their retrospective nature and the small number of patients involved. The reporting format is also different. In a French study of 195 PTAs in 151 patients with graft RAS, the initial success rate was 85%. There was 30% restenosis, and the restenosis rate after repeated PTA was 26%. The 5-year secondary patency rate was more than 85% [29]. In other papers with small study populations, technical success rates ranged from 81% to 94% [16,28,30], and clinical success rates ranged from 67% to 82% [10,16, 30]. In segmental branches, there is a lower success rate (67%); the primary patency is 58% and the secondary patency is 69% at a mean follow-up of 5.1 years [28]. The success rate is lower for anastomotic strictures [13]. Though the incidence of stenosis is similar between end-to-side anastomosis to the external iliac artery and end-to-end anastomosis to the internal iliac artery, PTA in the latter situation is technically more difficult and results in a higher complication rate and more graft loss [6].

It is very tempting to implant a renal stent to provide a good final picture before the patient leaves the angiographic suite. However, both the clinician and patient should understand the risk of late restenosis. There is no large series that identifies late restenosis in stents used in renal transplant. The number of patients receiving stents for RAS in renal graft is usually small and the studies are all retrospective. In a study involving seven patients followed for a median of 14.8 months, five remained normal and there were two with insignificant restenosis (< 35% and 50%). All had good blood pressure control [13]. In another six patients with a mean follow-up of 34 months, all stents were patent and there was one restenosis of less than 50% with no clinical significance [31]. Bertoni et al reported their results using Palmaz stents in nine patients followed for 1 to 3 years. There were significant drops in mean blood pressure and peak flow velocity in the renal artery, but no significant changes in serum creatinine [32].

One may get an idea of the long-term results of stenting by referring to the results with stents in native kidneys. A meta-analysis by Rees reported a 99% technical success rate after stent placement in 1,128 arteries [33]. Follow-up angiography of 563 arteries performed at a mean of 7.9 months showed 77% patency. Leertouwer et al showed 26% restenosis angiographically in 236 arteries at a mean follow-up of 19 months [34], which is not significantly better than the 30% restenosis after PTA in 515 patients reported by Rees. Though late restenosis may be treated using re-angioplasty, we are dealing with a solitary kidney and an unnecessary stent may mean a long nightmare for the patient. Thus, our policy is to try angioplasty first. If the result is radiologically less than satisfactory, but the pressure gradient is less than 15 mmHg, we follow the patient clinically, assess the blood pressure, and determine whether the dosage of antihypertensive drugs can be reduced or if there is any improvement in renal function. If the clinical response is not good, it may not be too late to intervene again.

Stent technology is always evolving, and there is continuing research and development to prevent restenosis after stenting. A recent promising technique involves drug-eluting stents. A sirolimus-coated stent has proven to be effective in preventing restenosis after stenting in coronary arteries and femoral arteries [35, 36]. Its use in the renal artery is still in the early experimental period, but if drug-eluting stents can be shown to reduce restenosis, it will be a milestone in endovascular intervention for renal transplantation.

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