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Two-stent strategy for renal artery stenosis with bifurcation lesion

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Abstract: Renal artery stenosis (RAS) with a bifurcation lesion is a challenge for interventional therapy. The aim of this study is to summarize our experience in RAS with a bifurcation lesion. Five patients with RAS involving bifurcation lesion are described. In cases 1 to 3, a single-stent strategy was first adopted. However, these three patients were converted to a two-stent strategy for bailout stent implantation in the side branches. In cases 4 and 5, a simultaneous kissing stent technique was performed. Angiography showed that the reference vascular diameter of the main branch was much larger than those of the side branches. Although obvious residual stenosis existed in cases 1 to 3 after stent implantation, no obvious residual stenosis was seen in cases 4 and 5. Renal artery duplex sonography was performed in cases 1 through 5 at 6, 7, 7, 8, and 6 months, respectively, after the procedures. No evidence of restenosis or occlusion was seen. In conclusion, stent implantation with the simultaneous kissing stent technique may result in more simple and more satisfactory immediate angiographic results.

Key words: Peripheral atherosclerotic artery disease, Angioplasty, Stents, Renal artery stenosis
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1 Introduction

Atherosclerotic renal artery stenosis (RAS) usually involves the ostium and the proximal one-third of the renal artery main branch. Occasionally, atherosclerotic RAS involves renal artery bifurcations (Misra *et al*., 2008; Zheng *et al*., 2010). Renal artery angioplasty with stent placement can safely and successfully resolve atherosclerotic narrowing, but stent implantation in atherosclerotic RAS involving bifurcation is not only troublesome, but also challenging.

One challenge in interventional therapy for RAS with bifurcation is to avoid side branch occlusion. Techniques developed in percutaneous coronary intervention might be used in these patients. Numerous techniques have been proposed for treating bifurcation coronary artery disease. These methods can be classified into one- and two-stent approaches, with the two-stent techniques including the T-stenting technique, the crush stenting technique, the simultaneous kissing stent technique, and so on (Rizik *et al*., 2008). Although studies from the bare-metal stent (BMS) era consistently demonstrated that the one-stent approach was superior to the two-stent approach (Al Suwaidi *et al*., 2001), this remains controversial in the drug-eluting stent (DES) era (Colombo *et al*., 2004; Pan *et al*., 2004). Although major adverse cardiac event rates with a single BMS were substantially less than those with more complex two-stent techniques (Al Suwaidi *et al*., 2001), this might not be true in renal artery stenosis, because renal vessels are often larger than coronary vessels in diameter. When abrupt closure of a side branch occurs and stenting becomes necessary to preserve branch patency, a two-stent strategy is unavoidable.

Another challenge is in-stent restenosis. In interventional therapy for RAS with bifurcation lesion, a small renal artery (reference vessel diameter less than 5.0 mm) is often involved. The main complication after stent treatment for RAS is in-stent restenosis. Some researchers have concluded that, in small renal arteries, there remains a considerable risk of restenosis on the order of 40% (Zähringer *et al*., 2008). A possible solution in small renal arteries might be DES, although this was not supported by the GREAT trial (Zähringer *et al*., 2008). In the GREAT trial, the in-stent percent diameter stenosis, binary restenosis rates, late lumen loss, and repeat revascularization after renal artery stent implantation were lower in the sirolimus-eluting stent group than in the BMS group, but the difference was not statistically significant, which might be explained by the number of target vessels with reference caliber ≥5.0 mm (Zähringer *et al*., 2007).

Using different strategies, we have treated five RAS patients with bifurcation lesions. The aim of this study is to summarize our experience in renal bifurcation lesions. Although the sample size is small, we think it worthwhile to appraise these data from a clinical perspective.

2 Patients and methods

2.1 Patient population

From January 2005 to March 2009, there were 208 patients with atherosclerotic RAS receiving renal artery stent implantation in our clinic centre, among whom there were five patients with a bifurcation lesion. Written informed consents were obtained from patients before their procedure. The clinical characteristics of the five patients are listed in Table 1.

2.2 Renal arteriography

Renal arteriography was performed through a femoral approach. The renal arteries were visualized in an anterior-posterior projection. In the renal artery with bifurcation, the upper polar branch was called side branch 1, and the lower polar branch was called side branch 2. The outer diameter of the angiographic catheter was used as a reference to measure the vessel diameter and minimal luminal diameters of the renal arteries. Severity of stenosis was calculated by the formula: $DS=(1-d_{min}/d_{ref})\times100\%$, where DS is the diameter stenosis, d_{min} is the minimal luminal diameter, and d_{ref} is the reference diameter. Existence of a renal artery lesion with ≥50% diameter stenosis was considered RAS. Renal arterial lesions with eccentric mural irregularity of stenosis in ostium and the proximal one-third segment of the renal artery were deemed atherosclerotic RAS. Renal arterial lesions exhibiting characteristic circumferential, beaded mural irregularity with or without associated stenosis or aneurysm formation were labeled fibromuscular

Table 1 Clinical characteristics and follow-up

Parameter	Characteristics				
	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	Female	Female	Male	Male	Female
Age (year)	73	66	53	76	69
Concomitant disease	AP, HTN	AP, HTN, DM	MI, HTN	MI, HTN	AP, HTN, CVD
Preoperation					
Cr (μmol/L)	139	124	94	138	82
Urea (mmol/L)	9.9	5.3	5.2	5.7	7.1
Follow-up					
Time (month)	6	24	30	8	6
Cr (μmol/L)	97	136	90	118	84
Urea (mmol/L)	7.9	3.0	5.0	6.8	8.7
Blood pressure (mmHg)					
Preoperation	180/110	170/100	120/65	110/90	170/90
Follow-up	140/80	160/100	130/85	115/75	130/85
Antihypertensive medication					
Preoperation	Nifedipine	Metoprolol, terazosin, amlodipine	Metoprolol, nifedipine, hydrochlorothiazide	Metoprolol, benazepril	Metoprolol, benazepril
Follow-up	Lercanidipine, losartan	Hydrochlorothiazide, terazosin, metoprolol	Metoprolol	Metoprolol, valsartan	Metoprolol, amlodipine

AP: angina pectoris; HTN: hypertension; DM: diabetes mellitus; MI: myocardial infarction; CVD: cerebrovascular disease dysplasia. All five patients here were diagnosed with atherosclerotic RAS.

2.3 Stent implantation

Stent implantation was performed in patients with RAS ≥70% with hypertension or abnormal serum creatinine concentration. Among the five patients, four had unilateral RAS and one had bilateral RAS. Individual details about each patient and the procedure are listed in Table 2. Case 4 was a bilateral RAS patient, with a left RAS with no bifurcation lesion, resolved by a 6.5 mm×15 mm hippocampus stent, and a right RAS with a bifurcation lesion. Residual stenosis after treatment was calculated by the formula: $(1-d_{res}/d_{ref})\times100\%$, where d_{res} is the residual lumen diameter.

Table 2 Procedure of stent implantation in renal artery bifurcation

Parameter	Procedure				
	Case 1	Case 2	Case 3	Case 4	Case 5
Bifurcation classification					
Stenosis	Right: side branch 1, 90%; side branch 2, 40%	Right: main branch, 50%; side branch 2, 95%	Left: side branch 2, 90%	Right: main branch, 70%; side branch 2, 70%	Left: main branch, 80%; side branch 1, 80%; side branch 2, 85%
Classification	Duke: type D; Lefevre: type 1	Duke: type F; Lefevre: type 1	Duke: type B; Lefevre: type 4a	Duke: type F; Lefevre: type 1	Duke: type D; Lefevre: type 1
d_{ref} (mm)	Main branch: 2.0; side branch 1: 3.0; side branch 2: 4.1	Main branch: 5.4; side branch 1: 4.0; side branch 2: 3.0	Main branch: 5.3; side branch 1: 3.3; side branch 2: 3.3	Main branch: 5.9; side branch 1: 3.4; side branch 2: 4.0	Main branch: 6.0; side branch 1: 3.5; side branch 2: 3.6
Guiding catheter	7FJR4	7FJL4	7FJR4	7FJR4	7FJR4
Wire	BMW, BMW	Whisper, BMW	BMW, BMW	BMW, BMW	BMW, BMW
Predilation		Side branch 2: Invatec, 3.5 mm×10 mm, 18 atm	Side branch 2: Pleon, 3.0 mm×20 mm, 8 atm		
1st stent	Side branch 1: Partner, 3.0 mm×15 mm, 18 atm	Side branch 2: Firebird 2, 3.5 mm×29 mm, 16 atm	Side branch 2: Partner, 3.5 mm×12 mm, 10 atm		
Kissing balloon	Invatec, 3.0 mm×10 mm, Sprinter RX, 3.5 mm×15 mm, 8 atm	Extensor, 3.0 mm×10 mm, 16 atm, stent dilation, 16 atm			
Arteriography	Ostium of side branch 2: stenosis of 75%	Main branch: stenosis of 50%; side branch 2: no obvious stenosis	Ostium of side branch 1: stenosis of 90%		
2nd stent	Main branch-side branch 2: Partner, 4.0 mm×15 mm, 18 atm	Main branch-side branch 1: Firebird 2, 4.0 mm×13 mm, 22 atm	Main branch-side branch 1: Partner, 3.5 mm×15 mm, 10 atm		
Simultaneous kissing stent technique				Partner, 12 atm, 3.5 mm×29 mm; Partner, 12 atm, 4.0 mm×29 mm	Excel, 12 atm, 3.5 mm×18 mm (×2)
Arteriography	Ostium of side branch 1: stenosis of 70%	Residual stenosis of 20% in ostium of side branch 2	Residual stenosis of less than 20% in ostium of side branch 2	No residual stenosis	No residual stenosis

d_{ref}: reference vessel diameter; BMW: balance middleweight universal, Abbott Vascular; Invatec: percutaneous transluminal coronary angioplasty (PTCA) dilation catheter, Invatec S.R.L.; Pleon: PTCA dilation catheter, Biotronik GmbH & Co.; Sprinter RX: PTCA dilation catheter, Medtronic Inc.; Extensor: PTCA dilation catheter, Medtronic Inc.; Partner stent: sirolimus-eluting coronary stent system, Lepu Medical Technology (Beijing) Co., Ltd.; Firebird 2 stent: sirolimus-eluting coronary stent system, MicroPort Medical (Shanghai) Co., Ltd.; Excel stent: sirolimus-eluting coronary stent system, JW Medical (Shandong) Co., Ltd.; 1 atm=101.325 kPa

2.3.1 Procedure in cases 1 to 3

After selective renal arteriography was performed, a 7F guide catheter was used to engage the origin of the renal artery, and one or two 0.036-cm wires were placed into the branch vessels distally. The angioplasty balloon was mounted on the wire and angioplasty was performed in the main branch and/or side branches. The stent was loaded onto the wire, and advanced across the atherosclerotic stenosis in one of the branches, and then deployed. The kissing balloon technique was performed if a significant stenosis appeared in another branch. For bailout stent implantation, another stent was loaded on another wire and advanced into the compressed vessel, then deployed. The kissing balloon technique was performed for post-dilation. In these patients, a one-stent strategy was the initial default strategy, but was converted to a two-stent technique if bailout of the side branch was necessary. The procedure in case 1 is shown in Fig. 1.

2.3.2 Procedure in cases 4 and 5

After selective renal arteriography was performed, a 7F guide catheter was used to engage the origin of the renal artery. Two 0.036-cm wires were placed into each branch vessel and two stents in a kissing fashion were deployed simultaneously in the main branch and side branches. The procedure in case 5 is shown in Fig. 2.

During the procedure, all patients were given a bolus of heparin intravenously (8000–10000 U), and received percutaneous coronary interventional therapy. Since the severity of stenosis at bifurcation was at least 70%, with main branch and side branches involved simultaneously, a pressure wire was not used. After the procedure, patients were given 75 mg/d clopidogrel for a minimum of 12 months.

2.4 Follow-up

The five patients were followed in the outpatient

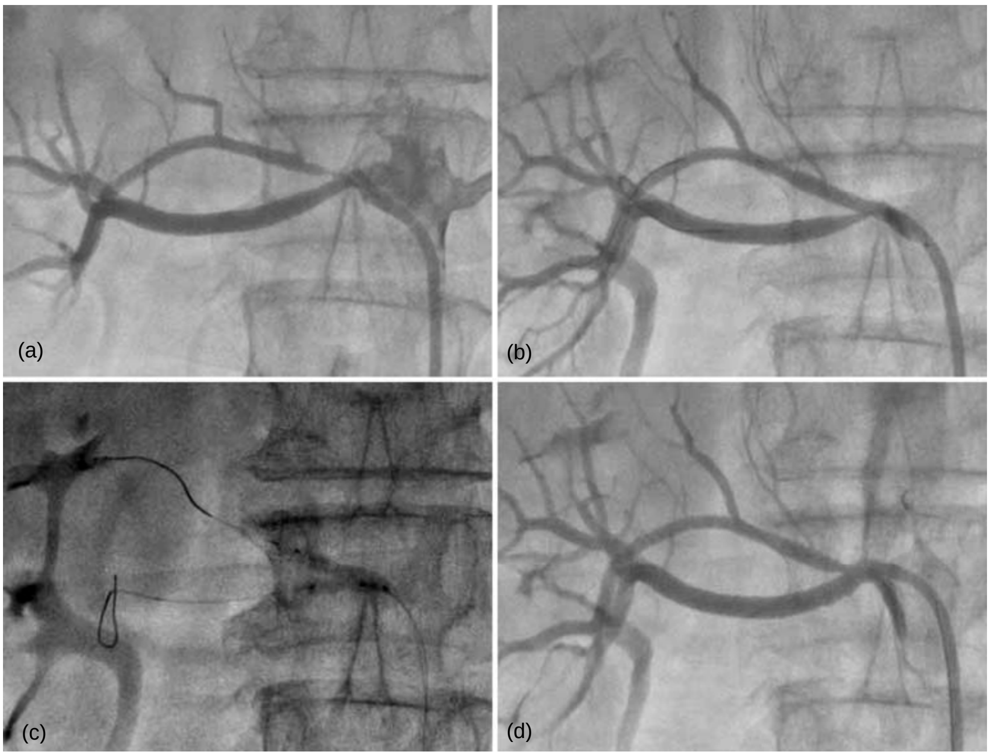

Fig. 1 Stent implantation in case 1

(a) Renal arteriography showed a 90% stenosis at the ostium of side branch 1 and a 40% stenosis at the ostium of side branch 2; (b) After stent (Partner, 3.0 mm×15 mm) implantation in side branch 1, a 90% stenosis at the ostium of side branch 2 appeared; (c) Kissing balloon technique was performed at the bifurcation (Invatec, 3.0 mm×10 mm, Sprinter RX, 3.5 mm×15 mm, 8 atm (1 atm=1.01325×10^5 Pa)); (d) After bailout stent implantation (Partner, 4.0 mm×15 mm) at the ostium of side branch 2, a 70% stenosis appeared at the ostium of side branch 1

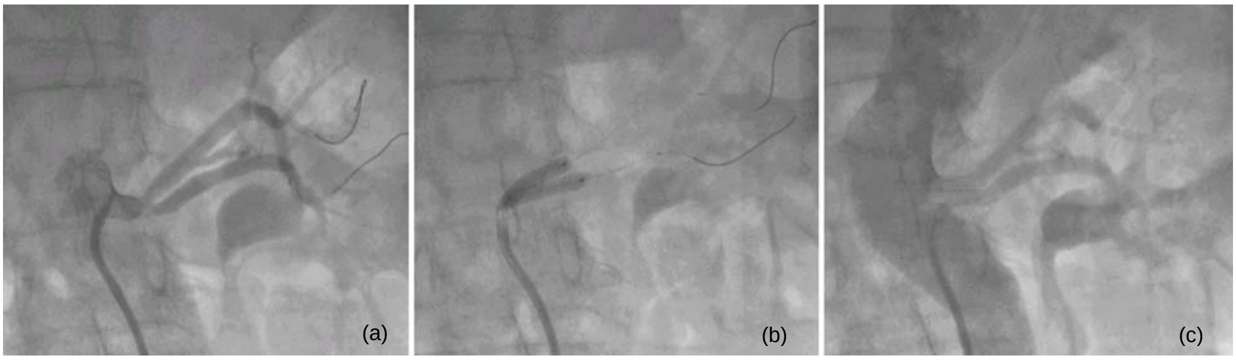

Fig. 2 Simultaneous kissing stent technique in case 5

(a) Renal bifurcation with a stenosis of 80% to 85%; (b) Positioning two stents (Excel, 3.5 mm×18 mm; Excel, 3.5 mm×18 mm) simultaneously at the main branch and side branches, and the proximal portions of the stents forming a double barrel; (c) After stent implantation, angiography showed no residual stenosis

department or by telephone. Symptoms, blood pressure, medication use, and serum creatinine were recorded, and renal artery duplex sonography was performed. Restenosis was defined as a peak systolic velocity of more than 2 m/s and a difference of more than 0.05 between resistive indexes.

2.5 Statistical analysis

Data are presented as mean±SD or numbers of patients and percentages.

3 Results

3.1 Angiography, angioplasty, and stent implantation

As shown in Table 2, the renal artery reference vessel diameters of the main branch, side branch 1, and side branch 2 were (5.6±0.4), (3.4±0.4), and (3.6±0.5) mm, respectively. The reference vessel diameter of the main branch is much larger than those of the side branches.

In cases 1 to 3, another side branch ostium was compressed after the stent implantation of one side branch. Thus, after dilation in both ostia by the kissing balloon technique, a second stent was deployed at the compressed side branch, but with residual stenosis in the side branches. In case 1, there was significant residual stenosis in side branch 1, although the kissing balloon technique was performed for post-dilation (Table 2).

In cases 4 and 5, the stenosis in bifurcations was treated by the simultaneous kissing stent technique. Two coronary stents were deployed simultaneously with no obvious residual stenosis.

3.2 Follow-up

As shown in Table 1, two patients (cases 1 and 5) had a decrease in blood pressure, three patients (cases 2, 3, and 4) had no significant change in blood pressure. Case 3 had a reduction in antihypertensive medications.

During follow-up, serum creatinine was lower in case 1, but there was no significant change in the other patients. Renal artery duplex sonography was performed in cases 1 to 5 at 6, 7, 7, 8, and 6 months, respectively, after stent implantation. No evidence of restenosis or occlusion of the renal artery with stent was seen.

4 Discussion

Our experience from these five patients is as follows: (1) the one-stent strategy, which might not be a good choice for renal bifurcation lesions, was converted to a two-stent strategy, as bailout of the side branch was necessary in the first three patients; and, (2) the simultaneous kissing stent technique was successful in the last two patients with a simplified procedure and satisfactory angiographic results.

Renal artery stent placement is the standard today, and substantially improves technical and long-term clinical outcomes compared with angioplasty alone. In a meta-analysis of 1322 patients, stent placement had a higher technical success rate and a lower restenosis rate than percutaneous transluminal renal angioplasty (98% vs. 77% and 17% vs. 26%, respectively; *P*<0.001), as well as a higher cure rate for hypertension (Leertouwer *et al*., 2000). Renal artery stenosis involving bifurcations is not in majority of clinical practices (Zheng *et al*., 2010), and as a result, experience in treating renal artery bifurcation is limited. Interventional cardiologists have developed a number of techniques, hoping to achieve long-lasting results in complex lesion subsets, including coronary bifurcations (Rizik *et al*., 2008). These techniques might be used in renal artery bifurcations. In percutaneous coronary intervention for bifurcation, procedural shortcomings have included the inability to adequately cover the side branch ostium in bifurcation, stent distortion, redundancy of metal at the carina of the lesion, leading to increased incidence of ostial side branch restenosis, stent thrombosis, and subsequent target lesion revascularization (Rizik *et al*., 2008). All these are potential problems with interventional therapy for renal artery stenosis.

Challenges in stent implantation for renal bifurcation are as follows: (1) as in the five patients presented, the main branch diameter is larger than both side branch diameters and no stents can meet different vessel diameters simultaneously for both vessels; (2) balloon dilation or stent implantation in one branch can easily lead to ostium stenosis or occlusion of another side branch; (3) side branches are often small renal arteries (reference vessel diameter less than 5.0 mm) and have a relatively high in-stent restenosis rate; and, (4) undersizing the main branch balloon during the final kissing inflation leads to distortion of the main branch stent, causing suboptimal expansion and apposition of the main branch stent (Rizik *et al*., 2008). Incomplete stent apposition can lead to thrombosis and in-stent stenosis.

Because studies from the BMS era consistently demonstrated that the one-stent approach was superior to the two-stent approach (Al Suwaidi *et al*., 2001), and this was yet controversial in the DES era (Colombo *et al*., 2004; Pan *et al*., 2004), we first adopted the one-stent strategy for renal lesions with bifurcation, as was done in cases 1 to 3. All the three patients were finally converted to a two-stent strategy, because bailout stent implantation was performed to resolve compression or occlusion of the side branch, after which kissing post-dilation was performed. In cases 4 and 5, interventional therapy for renal artery stenosis with bifurcation was resolved by the simultaneous kissing stent technique. The strategy of simultaneous stent deployment consists of positioning two stents simultaneously, the proximal portions of the stents forming a double barrel in the main branch and forming a neocarina with or without predilation. Compared with cases 1 to 3, the procedures were simplified in cases 4 and 5, and angiographic results were ideal with no residual stenosis. This technique is best suited for lesions where the main branch diameter is larger than both daughter branches (Misra *et al*., 2008). Although angiographic results in cases 2 and 3 were acceptable, it seems that the simultaneous kissing stent technique is another reasonable or better strategy for renal artery with bifurcation. Advantages of this technique include simplicity, uninterrupted wire access to both branches, and no need for crossing through the side of a stent for final balloon inflations. Meanwhile, its disadvantages include the problem of a proximal edge dissection. If a proximal dissection does occur, the double barrels can be extended proximally with two more stents, or the V-stent can be converted to a crush by compressing the side branch stent with a main branch balloon. The side branch is then reaccessed and redilated with a kissing inflation, and finally, a proximal bailout stent is implanted (Colombo *et al*., 2004; Rizik *et al*., 2008). Although the angiographic results were better in cases 4 and 5, gaps may exist between the dilated stent and vessel walls, as cross-sections of the dilated stent balloon were two circles. This might lead to worse apposition, thrombosis, and restenosis.

No evidence of deterioration of renal function, thrombosis, restenosis, or occlusion was found during follow-up, which suggests the safety of stent implantation in renal bifurcations, though the procedures were complicated in some cases.

Another challenge in renal bifurcation is the involvement of a small renal artery. In-stent restenosis rates in small renal artery are much higher than those in other renal arteries (Lederman *et al*., 2001). We thought that DES might reduce the occurrence of restenosis, as has been demonstrated in the coronary artery. Recently, we reported the safety and efficacy of coronary DES for atherosclerotic stenosis of small renal arteries. In that study, no evidence of in-stent restenosis was found in 25 patients with small renal arteries after coronary DES treatment during a follow-up period of six months (Li *et al*., 2009). The safety and efficacy of coronary DES in renal artery have also been reported by Ge *et al*. (2010).

However, there are still some limitations in our study. Renal artery angiography was not performed during follow-up in our study. Although there was no observed evidence of in-stent restenosis by duplex sonography, significant in-stent intima hyperplasia could not be excluded because of the sensitivity of duplex sonography. For example, duplex sonography had not detected the post-procedure residual stenosis in side branches in this study. Again, limited patient numbers may also limit our findings.

5 Conclusions

Preliminary experience shows that a two-stent strategy can be used safely in renal bifurcation lesions, and the simultaneous kissing stent technique, which has been used in coronary intervention, might be a simple and effective strategy.

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