Endovascular Therapy Using Diluted Contrast Medium for Critical Limb Ischemia in a Patient with Chronic Kidney Disease

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Summary
A high percentage of patients with critical limb ischemia have concurrent chronic kidney disease (CKD). However, endovascular therapy (EVT) can be problematic in CKD patients because the use of a large volume of iodinated contrast medium is associated with an increased risk of contrast-induced nephropathy (CIN).1 We developed a method of EVT using digital subtraction angiography (DSA) with diluted contrast medium (low-concentration DSA). Herein, we report a case in which EVT with low-concentration DSA achieved revascularization while preserving the patient’s renal function.

Case Report
An 88-year-old woman with progressive rest pain, ulceration, and necrosis of both lower limbs (Figure 1) was referred to our institution for revascularization. At presentation, the patient had hypertension, atrial fibrillation, chronic heart failure, and CKD. Her height was 150 cm and her weight was 40.4 kg. Initial serum urea nitrogen was 53 mg/dL and creatinine was 4.36 mg/dL. The patient’s estimated glomerular filtration rate (eGFR) was only 7.9 mL/minute/1.73 m². Her left ventricular ejection fraction was approximately 40%, with diffuse hypokinesis of the heart wall. Her serum brain natriuretic peptide was 1773.0 pg/mL, while the patient’s ankle-brachial index was 0.58 on the right side and 0.79 on the left. Noncontrast magnetic resonance angiography revealed total occlusion from the right common iliac artery to the external iliac artery and left below-the-knee (BTK) lesions. However, details of BTK lesions could not be discerned because of poor image quality.

We first attempted to treat the chronic total occlusion of the right iliac artery. We deployed 2 SMART® stents (8.0/60 mm, 7.0/40 mm; Cardinal Health Japan, Tokyo, Japan) from the distal external iliac artery to the proximal common iliac artery with an intravascular ultrasound (IVUS)-guided approach using 7 mL of contrast medium. The patient’s right ankle-brachial index increased to 1.28 after this treatment.

Two weeks after the first session, EVT was performed for the BTK lesions on the left side. Due to the difficulty of applying only the IVUS-guided approach to BTK intervention, we performed EVT using an adjusted DSA program with diluted contrast medium to preserve renal function. Angiography was performed with an Allura Xper FD10 machine (Philips, Amsterdam, The Netherlands). We adjusted the DSA parameters and found that we could obtain acceptable images with a 1:10 dilution of contrast medium. The specialized parameters greatly increased the sensitivity of the angiographic images and en-
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Figure 1. Lower limbs of 88-year-old woman with chronic kidney disease. Both lower limbs show ulceration and necrosis.

Table. Comparison Between Standard DSA and LC-DSA

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<th>Standard DSA</th>
<th>LC-DSA</th>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>normal</td>
<td>high</td>
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<tr>
<td>Edge kernel</td>
<td>small</td>
<td>large</td>
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<tr>
<td>Contrast</td>
<td>1.0</td>
<td>4.5</td>
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<tr>
<td>Edge gain</td>
<td>3</td>
<td>1</td>
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DSA indicates digital subtraction angiography; and LC, low concentration.

hanced the contrast, resulting in high resolution. The parameters also lowered the edge strength caused by increased noise (Table). We used a preset diluted contrast solution containing 10 mL of iopamidol 300 mg/mL contrast medium (BYSTAGE 300; Teva Takeda Pharma Ltd., Aichi, Japan) and 90 mL of 5% glucose. The contrast medium was the same as that used in standard EVT. We manually injected approximately 5 to 10 mL of the diluted contrast medium per angiogram through the guiding catheter, which was positioned in the proximal popliteal artery. Control angiography with low-concentration DSA revealed total occlusion of the proximal anterotibial artery and posterotibial artery, as well as severe stenosis of the distal peroneal artery (Figure 2). The main vessels and small collaterals were clearly identified (Figure 2). The patient reported no pain caused by diluted contrast injection. We passed the chronic total occlusion in the anterotibial artery using a Gradius wire (Asahi Intec Co., Aichi, Japan) and a Prominent microcatheter (Tokai Medical Co., Aichi, Japan) using low-concentration DSA-guided antegrade wiring. Additionally, we used a Chevalier floppy wire (Cardinal Health Japan, Tokyo, Japan) in the peroneal artery. After ballooning both lesions, the final angiography showed acceptable flow to the left leg and the wound (Figure 3). We identified the main vessels and small branches and confirmed wound blush (Figure 3E). The total volume of contrast medium used was 20 mL, which was markedly less than that used in the conventional procedure, which usually requires approximately 100 mL or more of contrast medium. The dose area product was 6.9 Gy cm². Total procedure time was 44 minutes and fluoroscopic time was 21.1 minutes. The patient’s renal function was preserved (preprocedure eGFR, 7.9 mL/minute/1.73 m²; postprocedure eGFR, 12.3 mL/minute/1.73 m²) and she has not required hemodialysis in the 2 years since treatment. The patient’s skin perfusion pressure in the left dorsal region increased from 43 mmHg to 123 mmHg at approximately 1 week after the procedure. Following this intervention, minor amputation was performed by a plastic surgeon. The patient’s wound healed completely without worsening of renal function.

Discussion

EVT can be problematic in CKD patients. The procedure is associated with complications such as CIN,1) especially in patients with critical limb ischemia who require repeat interventions to achieve complete wound healing because of the high rate of restenosis in BTK lesions.2,3) The large volume of iodinated contrast medium often required in conventional EVT is associated with the risk of CIN.4)

Various methods for preventing CIN have been reported, including hydration, hemofiltration, intravenous administration of iloprost, and the use of ascorbic acid, nicorandil, or N-acetylcysteine.5-14) However, there is presently no gold standard method and CIN occurs in approximately 5%-18.5% of patients, even when preventive methods are applied. The most effective method to prevent CIN is contrast volume reduction.15) However, despite the dangers, many previous studies have used over 100 mL of iodinated contrast medium, except when performing carbon dioxide angioplasty.5-14)

EVT can be performed effectively with carbon dioxide angioplasty in CKD patients.16,17) However, this method is associated with severe complications and poor image quality.18) Carbon dioxide angiography results in poor imaging of BTK lesions because of gas bubbles. Moreover, patients often experience severe pain that may cause them to move their legs during the procedure. The quality of DSA image tends to be degraded by this lower limb
Figure 2. Control angiography. The main vessels and some branches are identified with low-concentration digital subtraction angiography. A: Control angiography from the diagnostic catheter located in the popliteal artery reveals total occlusion of the proximal anterotibial artery (ATA, arrow) and posterotibial artery (PTA, arrow). The peroneal artery is patent (PA, arrow). B: The black arrow indicates severe stenosis of the distal peroneal artery. C: Distal portion of below-the-knee artery. There are collaterals distal to the PTA (Collateral, arrow) D: Vessels below the ankle are readily identifiable. ATA indicates anterotibial artery; PA, peroneal artery; and PTA, posterotibial artery.

Figure 3. Final angiography. A: Final angiography from the guiding catheter located in the popliteal artery shows acceptable antegrade flow from the anterotibial artery to the dorsalis pedis artery. B-D: Vessels and collateral channels are readily identified. E: Wound blush is also identified (wound blush, arrow). DPA indicates dorsal pedis artery.
movement.

The IVUS-guided approach effectively reduces the amount of contrast medium required. However, it is difficult to determine the degree of blood flow as well as the number of branch vessels and collaterals when using IVUS. Furthermore, IVUS is difficult if the IVUS catheter cannot pass BTK lesions.

To resolve the problems associated with IVUS, we developed a DSA protocol with specialized diluted contrast medium. Previous studies have reported computed tomography angiography using diluted contrast at a dilution ratio of roughly 1.3 to 1.4. However, to our knowledge, there are no reports of intra-arterial DSA with diluted contrast medium. DSA with diluted contrast medium was very effective in preventing progression of renal dysfunction because the total volume of contrast medium was markedly less than that in the standard EVT procedure. Furthermore, the image quality yielded by DSA was acceptable (Figures 2 and 3). This method of DSA with diluted contrast medium produces angiographic images with very high sensitivity, enhanced image contrast, and reduced edge gain. Using the adjusted DSA parameters (Table), we obtained high-resolution angiographic images with diluted contrast medium. Generally, we use a 1:10 dilution of contrast medium because it is easy to prepare and results in satisfactory angiographic images, even in BTK vessels. A valuable advantage of DSA with diluted contrast medium is that no special devices are required if the DSA parameters are adjusted appropriately. Indeed, we used our routine angiography machine in the present case. The technique of angiography is the same as that for standard DSA. The frame rate is 3 frames per second. We usually prepare a preset diluted contrast medium containing 10 mL of contrast medium and 90 mL of 5% glucose, then we manually inject 5 to 10 mL of the diluted contrast medium. We use 5% glucose solution for dilution to avoid volume overload. We use an average of less than 1.0 mL of contrast medium per injection. Using this method, patients are often able to remain still since there is no pain associated with contrast medium injection, unlike with carbon dioxide angiography. We can identify main vessels and small channels with low-concentration DSA and can perform complex procedures, such as distal puncture or the trans-collateral retrograde approach.

Surgical bypass was also considered in this case. The strategy for arterial revascularization should be selected with consideration of the patient’s life expectancy and the availability of vein grafts. However, patients with critical limb ischemia tend to be in poor condition, with advanced age, frailty, and systemic disease, as in this case. In this case, we concluded that EVT was preferable to bypass surgery because of the risk of general anesthesia.

**Limitations:** Low-concentration DSA has some disadvantages. First, DSA imaging is very susceptible to motion artifacts because of its high sensitivity. Therefore, it is often difficult to apply this method to patients who move their legs spontaneously and to aortoiliac lesions because of intestinal movement. Second, imaging quality is dependent on the location of the angiogram. If the guiding catheter is too far from the DSA area, the angiography images tend to be faint. If imaging quality is unsatisfactory, adjustment of the location of the angiogram or the concentration of contrast medium is necessary. Third, this method cannot be used in patients with an allergy to contrast agent.

**Conclusions**

We successfully performed EVT for BTK lesions in a CKD patient using DSA with diluted contrast medium. We obtained clear angiographic images of the BTK lesions using a very small volume of iodinated contrast medium. EVT using low-concentration DSA was a very effective BTK intervention that preserved renal function in this CKD patient.

**Disclosures**

Conflicts of interest: The authors declare that there are no conflicts of interest.

**Research ethics:** All procedures were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Informed consent was obtained from the patient described in the case report.

**References**


