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The outcomes of carbon dioxide digital subtraction angiography for percutaneous transluminal balloon angioplasty of access circuits and venous routes in hemodialysis patients

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Abstract

The outcomes of carbon dioxide digital subtraction angiography (CO2-DSA) for performing percutaneous transluminal balloon angioplasty (balloon PTA) in hemodialysis patients has not been fully clarified. The purpose was to compare the outcomes of balloon PTA of hemodialysis shunts in terms of vessel patency between patients treated using CO2-DSA and conventional digital subtraction angiography using iodine contrast medium (C-DSA).

We retrospectively evaluated 76 patients (38 males and 38 females, mean age: 65.0 ± 14.0 years). They were under hemodialysis and treated with balloon PTA using CO2-DSA or C-DSA at our institution between 2009 and 2016. Mean duration of the follow-up period was 25.59 ± 21.45 months. We compared the patency rates obtained after CO2-DSA-based balloon PTA with those after C-DSA-based balloon PTA. Secondary patency, which was defined as the duration of patency after all further endovascular interventions until surgical repair, was considered as the endpoint in this study.

Overall, 19 and 57 patients underwent CO2-DSA- and C-DSA-based balloon PTA, respectively. CO2-DSA- and C-DSA-based balloon PTA produced clinical success rates of 100% and 96.5%, respectively. Blood vessel injury occurred in one patient who underwent C-DSA-based balloon PTA. No major complications occurred in CO2 group. At 24 months, the post-PTA secondary patency rates of CO2-DSA- and C-DSA-based balloon PTA were 94.1% and 93.9%, respectively ($P = .9594$).

CO2-DSA is safe for hemodialysis patients. Compared with C-DSA, CO2-DSA-based balloon PTA produces have a similar secondary patency rate.

Abbreviations: C-DSA = conventional digital subtraction angiography, CO2-DSA = carbon dioxide digital subtraction angiography, KDOQI = The National Kidney Foundation Kidney Disease Outcomes Quality Initiative, PTA = percutaneous balloon angioplasty.

Keywords: CO2, dialysis, DSA, interventional radiology, PTA

1. Introduction

One of the greatest challenges of hemodialysis is the limited durability of vascular access points. Thrombosis associated with venous stenosis due to neointimal hyperplasia is the most frequent complication, which results in the loss of the access for both autogenous (native arteriovenous fistulas) and non-autogenous (prosthetic grafts) arteriovenous access points.[1,2] The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) Vascular Access Guidelines state that percutaneous balloon angioplasty (balloon PTA) is the first-line treatment for access-circuit stenosis.[3–5]

For balloon PTA, conventional digital subtraction angiography (C-DSA) using iodine contrast medium is usually performed, but in cases with possible iodine allergy the use of iodine contrast is contraindicated. Carbon dioxide digital subtraction angiography (CO2-DSA) can be used as an alternative to C-DSA in such cases.

CO2 angiography was first developed by Hawkins in 1982.[6] The use of CO2-DSA has been studied extensively since the development of a safe and efficient CO2 delivery system.[7,8] Two of the most appealing characteristics of CO2 are that it is non-nephrotoxic and non-allergenic. CO2 angiography is generally used for minimizing the renal injury in the non-hemodialysis patients. Also, CO2 angiography has an important role to play in

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patients that are contraindicated for iodine contrast medium use.[6,7,9–11] If dialysis has already been performed, CO2-DSA is likely to be performed in patients that are contraindicated for iodine contrast medium. A previous report showed that CO2 is a useful contrast agent in the diagnosis and intervention of failing hemodialysis access, eliminating or limiting the use of iodinated contrast material.[12] However, the outcomes of CO2-DSA for performing balloon PTA in hemodialysis patients has not been fully clarified.

We have employed CO2-DSA for the patients in whom C-DSA was contraindicated because of iodine allergy. The purpose of this retrospective study was to compare the outcomes of percutaneous transluminal balloon PTA in terms of blood vessel patency between patients treated using CO2-DSA and C-DSA.

2. Methods

The institutional review board of Nagasaki University Hospital approved this retrospective study on August 21, 2018 (approval number: 18082022), and no individual patient consent was required. A written informed consent for the PTA procedure and its possible complications was obtained from each patient. This study was conducted in accordance with the Declaration of Helsinki.

2.1. Patients

We retrospectively evaluated 76 patients (38 males and 38 females, mean age: 65.0 ± 14.0) who had at least 1 month of follow-up data. All patients were already on hemodialysis. They underwent balloon PTA using CO2-DSA (n = 19; the CO2-DSA group) or C-DSA (n = 57; the C-DSA group) at our institution.

Balloon PTA was performed in end-stage renal failure patients with hemodynamically significant stenosis (>50%) of the hemodialysis access circuit (autogenous fistulas or prosthetic grafts) or venous route. CO2-DSA was used in all 19 patients that were suspected or likely to iodine allergy.

2.2. PTA technique and follow-up

Interventional radiologists performed all of the procedures under local anesthesia (1% lidocaine). During the initial balloon PTA procedure in each case, the brachial artery was antegradely punctured with a 22-G needle (Medikit, Tokyo, Japan), and DSA was performed. After confirming the location of the stenotic lesion, a 5–6F sheath (Terumo, Tokyo, Japan or Mosquito; Boston Scientific, Watertown, MA) was antegradely inserted into the brachial artery. After the intravenous administration of 1000 U heparin (Ajinomoto, Tokyo, Japan), 4- to 6-cm-long conventional balloons (Coyote and Synergy; Boston Scientific, Massachusetts), which were rated as having a burst pressure of 12 to 16 atm and an inflated diameter of 4 to 10 mm, were used. The target lesion was crossed with a 0.035-inch guidewire (Radifocus; Terumo, Tokyo, Japan), over which the balloon was introduced. Each balloon was inflated to a level below the rated burst pressure recommended by the manufacturer until the waist of the balloon had disappeared, before being inflated for 60 s. If the balloon waist remained visible after the balloon had been inflated at the rated burst pressure, the inflation procedure was terminated, and no further attempts were made. At the end of the procedure, the final DSA images were obtained.

The mean duration of the follow-up period was 25.59 ± 21.45 months. During the follow-up period, clinical examinations, dialysis access point venous pressure measurements (during dialysis), and measurements of dialysis access recirculation were planned every 4 weeks. DSA was performed every 3 months after the first balloon PTA procedure. Follow-up DSA was performed by puncturing the target blood vessel on the arterial side of the previous stenosis site using a 22-G needle (Medikit). If the stenosis had progressed, re-PTA was then performed.

2.3. CO2-DSA

Fixed angiographic equipment (Siemens Medical Solutions, Forchheim, Germany) and a CO2-imaging package were used in all cases in which CO2-DSA or C-DSA was performed.

Our CO2-DSA technique is as follows. A sterile bag attached to a tube with a stopcock is inflated with CO2. The bag is purged and inflated with CO2 3 times to eliminate contaminating room air. The stopcock is then closed, cutting off the connection to the inflated bag, and a tube with a 1-way valve is connected to a sidearm. The sidearm of the tube is connected to a 30-mL lock syringe.

The 30-mL lock syringe is then converted to a 10-mL syringe. The 10-mL lock syringe is filled and purged at least 3 times before the manual injection procedure. These steps create a closed CO2 system. The manual injection of CO2 is performed at a rate of 10 mL/s during the digital subtraction imaging.

High frame rates of 6 frames per second and stacking technology are required to produce adequate images.

2.4. Assessment

The procedural details were recorded, including the access type, the location and degree of the stenosis, details of the outcomes of the angioplasty procedure, and complications. The diameter of the adjacent segment of normal vein was used as the reference diameter. The percentage stenosis was defined as the maximum reduction in diameter compared with the diameter of the reference vessel.

The procedure outcomes were classified according to the criteria published by the Society of Interventional Radiology.[13] Clinical success was defined as the resumption of normal dialysis for at least one session. Primary patency was defined as the interval from the initial PTA until the second PTA. Secondary patency was defined as the duration of patency after all further endovascular interventions until surgical repair.

2.5. Statistical analysis

Statistics were performed to assess whether there were differences in various factors between two groups. Ages was expressed as the mean. Categorical variables were described as absolute values and percentages, which were compared with the χ^2 test or Fisher's exact test, as appropriate. The Mann–Whitney *U* test was used to compare continuous variables.

Primary and secondary patencies were assessed via Kaplan–Meier analysis. The log-rank test was used to determine statistical significance for comparisons between the two groups. *P*-values of $<.05$ were considered statistically significant. All statistical analyses were performed with the software JMP (SAS Institute, Cary, NC).

Table 1

Demographic characteristics of the study population.

Parameter	CO2-DSA n = 19	C-DSA n = 57	P
Age, y ± SD	62.0 ± 10.7	67.8 ± 10.9	.0467
Female gender, n (%)	11 (58)	27 (47)	.597
Risk factors			
BMI > 25	5 (26)	13 (23)	.7556
Hypertension, n (%)	12 (63)	44 (77)	.2431
Diabetes mellitus, n (%)	3 (16)	21 (37)	.1525
Dyslipidermia, n (%)	2 (11)	10 (18)	.719
Coronary artery disease, n (%)	2 (11)	14 (25)	.3297
Valve disease, n (%)	3 (16)	11 (19)	.7326
Cerebrovascular disease, n (%)	7 (37)	14 (25)	.3763
Peripheral arterial disease, n (%)	4 (21)	9 (16)	.5978
Atrial fibrilation, n (%)	3 (16)	10 (18)	.8604
Depression, n (%)	9 (47)	12 (21)	.359
Current smoker, n (%)	7 (37)	20 (35)	.8899
COPD, n (%)	3 (16)	8 (14)	.8502
Gout, n (%)	4 (21)	9 (16)	.5978
Clinical factors			
Arteriovenous fistulas (AVFs), n (%)	17 (89)	49 (85)	1
Medications			
Antipalte, n (%)	12 (63)	30 (53)	.595
Statin, n (%)	2 (11)	8 (14)	1
Oral antidiabetic, n (%)	1 (5)	9 (16)	.4356
Insulin, n (%)	2 (11)	13 (23)	.3302

BMI = body mass index, COPD = chronic obstructive pulmonary disease, SD = standard deviation.

3. Results

The demographic and clinical characteristics of the two groups are summarized in Table 1. The patients that were treated using CO2-DSA-based balloon PTA were younger than those treated using C-DSA-based balloon PTA ($P = .0467$).

Blood vessel injury occurred in one patient who underwent C-DSA-based balloon PTA. The patient was successfully managed by inflation of the balloon at low pressure combined with external manual compression for about 3 min. No major angioplasty-related complications were recorded in CO2-DSA group.

In the C-DSA group, 57 patients (30 males, 27 females) with 57 stenoses underwent balloon PTA. The 57 stenoses consisted of 47 venous stenoses, 7 stenoses affecting graft-to-vein anastomoses, 2 intragraft stenoses, and 1 stenoses affecting arterial anastomoses. The clinical success rate was 96.5% (55/57).

In the CO2-DSA group, 19 patients (8 males, 11 females) with 19 stenoses underwent balloon PTA (Fig. 1). The 19 stenoses consisted of 16 venous stenoses, 1 stenoses affecting graft-to-vein anastomoses, 1 intragraft stenosis, and 1 stenosis affecting an arterial anastomosis. The clinical success rate was 100% (22/22).

The mean durations of the C-DSA- and CO2-DSA-based angioplasty procedures were 54.9 and 46.8 min, respectively ($P = .4377$).

No significant differences in the degree of stenosis before angioplasty or the diameter of the balloon used were detected between the C-DSA and CO2-DSA groups (Table 2). No significant differences in the percentage improvement in blood vessel diameter seen after the angioplasty procedure were detected between the C-DSA and CO2-DSA groups in cases of venous stenosis ($P = .2456$) or total cases ($P = .0650$) (Table 2).

Information regarding inflated balloon diameter and the inflation pressure used are provided in Table 3. The inflated balloon diameter in CO2-DSA group was significantly smaller that of C-DSA group in cases of venous stenosis ($P = .0296$) and in total cases ($P = .049$). The inflation pressure in CO2-DSA group was significantly higher that of C-DSA group in cases of venous stenosis ($P = .0095$) and in total cases ($P = .0334$).

Kaplan–Meier analysis was used to assess the primary and secondary patency rates of each group. The primary patency rates at 12, 24, and 36 months were 3.6%, 1.8%, and 0%, respectively, in the C-DSA group, whereas all of these rates were 0% in the CO2-DSA group ($P = .1237$). The mean duration of the primary post-PTA patency period was 4.1 ± 3.7 and 3.5 ± 2.1 months in the C-DSA and CO2-DSA groups, respectively ($P = .3047$).

The secondary patency rates at 12, 24, and 36 months were 93.9%, 93.9%, and 89.0%, respectively, in the C-DSA group, whereas all of these rates were 94.1% in the CO2-DSA group ($P = .9594$) (Fig. 2). The mean duration of the secondary post-PTA patency period was 24.32 ± 23.48 and 26.02 ± 20.93 months in the CO2-DSA and C-DSA groups, respectively ($P = .5768$).

4. Discussion

In this study, there was no significant difference in the secondary patency rate of hemodialysis shunts after balloon PTA between

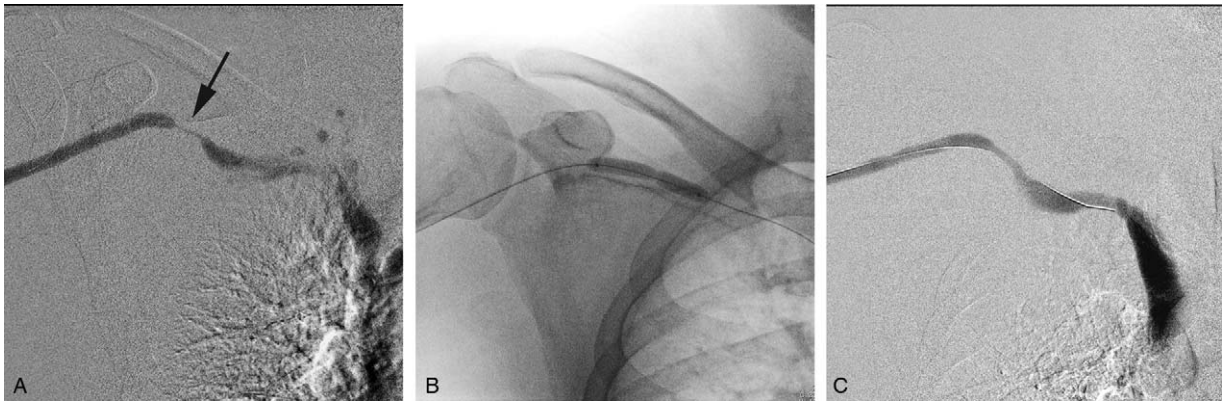

Figure 1. Anteroposterior venograms of the right subclavian vein in a 46-year-old female with hemodialysis failure. (A) CO2-DSA showed severe stenosis (arrow) of the right subclavian vein. (B) The right subclavian vein was dilated with a 6-mm balloon catheter. (C) After the balloon PTA procedure, CO2-DSA showed that the stenosis in the right subclavian vein had improved.

Table 2

Percentage diameter stenosis before PTA, residual percentage diameter stenosis after PTA, and percentage diameter improvement after PTA.

	Percentage diameter stenosis before PTA (%)			Residual percentage diameter stenosis after PTA (%)			Percentage diameter improvement after PTA (%)		
Stenosis type	CO2-DSA	C-DSA	*P*	CO2-DSA	C-DSA	*P*	CO2-DSA	C-DSA	*P*
Venous	83.1±11.5	82.3±11.8	.8652	45.3±18.0	39.1±20.1	.2317	37.8±17.8	43.2±20.9	.2456
Graft-to-vein anstomotic	70	85.7±11.3	–	55	35.0±30.1	–	15	50.7±25.2	–
Intragraft	95	95±0	–	70	45±35.4	–	25	50±35.4	–
Arterial anastomotic	95	95	–	70	70	–	25	25	–
Total	83.7±11.6	83.4±11.7	.9852	48.4±18.2	39.3±21.8	.0814	35.3±17.4	44.0±21.5	.065

Table 3

Diameter and loaded maximum pressure of balloons.

	Inflation diameter of balloon (mm)			Loaded maximum pressure (atm)		
Stenosis type	CO2-DSA	C-DSA	*P*	CO2-DSA	C-DSA	*P*
Venous	7.2±1.7	8.8±2.6	.0296	10.1±2.6	7.6±3.3	.0095
Graft-to-vein anstomotic	6	6.0±1.0	–	8	7.4±2.0	–
Intragraft	4	5.5±0.7	–	6	8.5±4.9	–
Arterial anastomotic	5	5	–	2	7	–
Total	6.8±1.8	8.2±2.6	.049	9.4±3.1	7.6±3.2	.0334

the CO2-DSA and C-DSA groups. In addition, no angioplasty-related complications were recorded in the CO2-DSA group. This study showed that CO2-DSA is safe and can be used as an alternative to C-DSA in balloon PTA for hemodialysis shunt. CO2-DSA has been shown to be an option in cases where the contrast agent is contraindicated, and is considered to be a useful method for future treatment. It also seems to lead to the expansion of indications for PTA treatment.

In the present study, there was no significant difference in the primary patency rate between the CO2-DSA and C-DSA groups ($P=.1237$). In addition, the primary patency rates of both groups were lower than those described in previous reports.[14–16] We performed balloon PTA in any stenosis which were found on follow-up DSA in every 3 months. This has resulted in higher frequency of re-PTA and better secondary patency rates compared with those of previous reports.[14–16] If sufficient secondary patency is achieved, patients benefit greatly because dialysis can be performed without surgical intervention. Post-PTA secondary patency is the most important outcome for patients because it represents the functionality of their vascular access sites. The secondary patency rates in this study were higher than in the past literatures, and the follow-up every 3 months may have led to good results.[14–16] However, this proof seems to need further research.

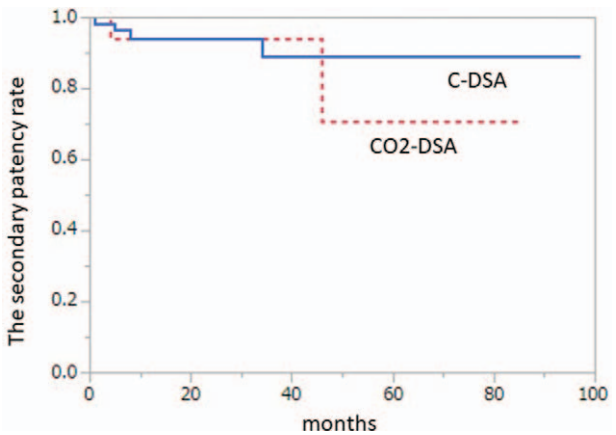

Figure 2. Graph showing Kaplan–Meier survival analysis of the secondary patency rates in patients who underwent CO2-DSA- or C-DSA-based balloon PTA. The secondary patency rates at 12, 24, and 36 months were 93.9%, 93.9%, and 89.0%, respectively, in the C-DSA group, whereas all of these rates were 94.1% in the CO2-DSA group ($P=.9594$).

In this study, the inflated balloon diameter was smaller and pressure in CO2-DSA group was significantly higher than those of C-DSA group in cases of venous stenosis and in total cases. Several studies have shown that the degree of stenosis is consistently overestimated by CO2 venography.[7,17,18] Such overestimation can occur because CO2 begins to dissolve in the blood immediately after injection to the vessels, and slow blood flow accentuates this process as it results in a longer period of blood-gas contact.[7,17,18] Therefore, the aforementioned result might suggest that stenosis was overestimated to a greater extent during CO2-DSA than during C-DSA, and so stronger pressure and smaller diameter might have been applied to the stenotic sites in the CO2-DSA group.

4.1. Limitation

Our study had several limitations. First, the number of patients was relatively small. Especially, the number of subjects in the CO2-DSA group was small. Second, the subjects in the CO2-DSA group were significantly younger than those in the C-DSA group ($P=.01$). A few studies have indicated that older age does not affect the patency rate,[14,15] but the possibility that the aforementioned age difference affected our results cannot be ruled out.

4.2. Future direction

Thus, further studies on a larger scale are needed. Further studies are needed to clarify age difference.

In conclusion, CO2-DSA is safe for hemodialysis patients. Compared with C-DSA, CO2-DSA-based balloon PTA produces have a similar patency rate and is an alternative to C-DSA-based produces for patients.

Author contributions

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