Effectiveness of high flow-volume intermittent hemodiafiltration during and after intervention to prevent contrast-induced nephropathy in patients with advanced chronic kidney disease: A pilot study

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Abstract

Objectives: We analyzed the effect of high flow-volume intermittent hemodiafiltration (HF-IHDF) on patients with advanced chronic kidney disease (CKD) undergoing procedures requiring administration of contrast medium.

Background: There is no effective method for preventing contrast-induced nephropathy (CIN), especially in patients with advanced CKD. We established HF-IHDF as a renal protective therapy with a filtration flow rate up to 5 times greater than standard continuous HDF. In this study, we tested whether HF-IHDF could prevent CIN in patients with advanced CKD more effectively than saline hydration only.

Methods: We retrospectively analyzed the incidence of CIN and clinical outcomes up to 1 year after performance of a procedure in 76 patients with advanced CKD. HF-IHDF was performed from just before the procedure until 2.5 hr after it. Hydration with 0.9% saline was also administered.

Results: The incidence of CIN was significantly lower in the HF-IHDF group than the saline group 2–3 days (0%, 0/76 patients vs. 9.3%, 5/54 patients; p < .05) and 1 month (3.9%, 3/76 patients vs. 14.8%, 8/54 patients; p < .05) after intervention. No difference between the two groups was detected in the proportion of patients requiring permanent hemodialysis within 1 year after intervention or the 1 year mortality rate. However, the number of patients free from progression of renal dysfunction after 1 year of follow-up was significantly higher in the HF-IHDF group (86.8%, 66/76 patients vs. 64.8%, 35/54 patients; p < .01).

Conclusions: HF-IHDF during and after interventional procedure requiring administration of contrast medium may prevent CIN in patients with advanced CKD.

Keywords
chronic, clinical trials, contrast agents, renal disease

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1 INTRODUCTION

Contrast-induced nephropathy (CIN) is a well-known cause of acute renal failure among hospitalized patients exposed to contrast medium during procedures such as contrast-enhanced computed tomography (CT), angiography, percutaneous coronary intervention (PCI), or percutaneous peripheral intervention (PPI). The occurrence of CIN itself is widely recognized to be associated with poor morbidity and mortality.1,2 Multiple risk factors for CIN have been described, and the stage of chronic kidney disease (CKD) is considered particularly important.3 Moreover, the incidence of CIN increases in proportion to the number of risk factors present in a patient.4,5 Because the number of patients with CKD has been increasing year after year, and CKD is recognized to be an independent risk factor for cardiovascular disease (CVD), the frequency of intervention in patients with advanced CKD (stage ≥3b) will likely increase substantially in the near future. Consequently, there should be adequate consideration regarding prevention of CIN by interventionalists. Hydration with 0.9% saline is widely recognized as a renal protective therapy under which the incidence of CIN is quite low for the patients with normal renal function (estimated glomerular filtration rate: eGFR ≥60 ml/min/1.73 m²).6,7 However, in patients with advanced CKD, saline hydration alone may not be sufficient to prevent CIN.8

Renal replacement therapy is another method aimed at preventing CIN in patients with advanced CKD. Whereas hemodialysis (HD) is considered ineffective or even harmful for the patients with stage G3 CKD,9,10 a recent study demonstrated that continuous hemofiltration (CHF) before, during, and after contrast exposure could prevent CIN in patients with stage G4 CKD by both filtering out the contrast medium and enabling administration of alkaline agents.11 Thus, CHF may be an effective new strategy for preventing CIN in patients with advanced CKD.

A limitation of CHF is that takes a long time (≥18 hr) due to its low removal efficiency. We therefore endeavored to establish a novel intermittent hemodiafiltration (IHDF) technique that increases the filtration flow rate up to 5 times compared to standard continuous hemodiafiltration (CHDF). Using this method in vitro, we demonstrated that the time required for 99% removal of contrast medium could be shortened to one-sixth of that necessary with standard CHDF.12 We termed this unique procedure high flow-volume intermittent hemodiafiltration (HF-IHDF) and have been applying this procedure clinically since 2008. In the present study, we tested whether HF-IHDF has a potential to prevent CIN in patients with advanced CKD (stage G3b or G4) receiving coronary angiography (CAG), PCI or PPI. Long-term prognosis, including renal function for up to 1 year after the intervention, was analyzed and compared to saline hydration only.

2 MATERIALS AND METHODS

2.1 Study population

We retrospectively analyzed 130 consecutive patients with advanced CKD (stage G3b or G4) who could be followed up for at least 1 month after an interventional procedure such as CAG, elective PCI or PPI. All of patients were treated at our center between April 2008 and December 2016 and were followed for up to 1 year without additional contrast exposure. As renal protective therapy, 54 patients were treated with saline hydration only (saline group), and 76 patients were treated with both saline hydration and HF-IHDF (HF-IHDF group). Patients with acute coronary syndrome, decompensated congestive heart failure, recent major bleeding, severe dehydration, or nephrosis were excluded from this study. Also excluded were patients on maintenance HD and those exposed to contrast medium within 3 months before the interventional procedure. The ethics committee of our hospital approved the protocol, and informed consent was obtained from all patients before the interventional procedure.

2.2 Study protocol

A summary of our study protocol is shown in Figure 1.

Before enrollment, all patients received blood tests over a period of at least 3 months in our outpatient clinic to confirm a fixed value for the estimated GFR (eGFR). The eGFR was calculated using the modified three-variable Modification of Diet in Renal Disease equation developed by the Japanese Society of Nephrology, which is adjusted for Japanese physical characteristics: eGFR = 194 × serum creatinine−1.094 × age−0.287 (if female, ×0.739).

Within 24 hr before the interventional procedure, blood tests to determine baseline parameters and echocardiography to assess the cardiac condition were performed in each patient. CKD stage was defined by the latest eGFR: G3b was 30 to 45 ml/min/1.73 m², and G4 was 15 to 30 ml/min/1.73 m². Anemia was defined using World Health Organization criteria; baseline hematocrit value <39% for men and <36% for women. Chronic heart failure was defined as left ventricular ejection fraction <40%, or a past history of treatment for decompensated heart failure.

Just after the entering the catheter room, a blood access UK catheter kit was percutaneously inserted through the common femoral vein. An extracorporeal circuit (TR-525, TORAY MEDICAL) generally used as a hemofilter for CHDF (EXCELFLO 1.3 m²; Asahi Kasei Kuraray Medical) and Sublood-BS (Fuso Pharmaceutical Industries, Ltd.), which served as the dialfiltrate and replacement fluid, were used during HF-IHDF. HF-IHDF was started just before each interventional procedure. Blood flow was maintained at 150 ml/min, filtration flow at 5,000 ml/hr, dialysate flow at 2,000 ml/hr, and replacement flow at 3,000 ml/hr (Figure 2a,b). The same flow rates were continued during the interventional procedure. Heparin was used as the anticoagulant in all patients during HF-IHDF. After each interventional procedure, blood in the extracorporeal circuit was returned to the patient. HF-IHDF was then restarted as soon as possible in the intensive care unit (ICU) for a fixed 150 min, which was the period needed to remove 90% of the contrast in an earlier in vitro examination.12 Body fluid removal was not performed during HF-IHDF.
In both the saline and HF-IHDF group, saline hydration at 1 ml kg⁻¹ hr⁻¹ was introduced 1–5 hr before the interventional procedure and was continued during the procedure and for 8–12 hr after it. Low-osmolarity contrast medium (iohexol 350 or iopamidol 370) was used during the interventional procedure in all patients. All patients were discharged from our hospital within 7 days, after it was confirmed that no complications were present.

Blood tests were performed 2–3 days and 1 month after the interventional procedure to check for CIN. Clinical follow-up to assess long-term prognosis, including mortality, and the need for permanent HD was continued for up to 1 year. Following examination for CIN at 1 month, four patients in the saline group and three patients in the HF-IHDF group were lost to follow up.

CIN was defined as an increase in the serum creatinine (sCr) concentration of more than 25% or 0.5 mg/dl from the baseline value. In addition, every patient underwent a medical examination for cholesterol crystal emboli based on the presence of typical features, including livedo reticularis, blue toe syndrome, or eosinophilia (eosinophils 400 ≥ counts/μl in peripheral blood). Pharmacotherapies being administered to the patients, particularly diuretics, angiotensin-converting enzyme inhibitors (ACE-Is), and angiotensin II receptor blockers (ARBs), were left unchanged during the perioperative period.

### 2.3 Risk scoring for incidence of CIN and requirement for in-hospital HD

Just after the interventional procedure, we evaluated the predicted likelihood of CIN and the requirement for in-hospital HD in each patient using the risk scoring proposed by Mehran et al.² When using saline hydration only as renal protection, older age (>75 years), anemia, diabetes, congestive heart failure, contrast medium volume, eGFR, and hypotension or use of an intra-aortic balloon pump (IABP) during the interventional procedure were considered independent risk factors for CIN or the need for in-hospital HD. After adding up the integer scores from these eight risk factors, we predicted the risks of CIN and need for in-hospital HD in all patients.

### 2.4 Statistical analysis

All results are presented as the mean ± SE or a percentage of the total value. Comparison of mean values between any two points were
made using Student’s t test. Analysis of variance (ANOVA) with post hoc Fisher’s test was used to compare categorical variables between the two treatment groups. Values of \( p < .05 \) were considered statistically significant.

### RESULTS

#### 3.1 Characteristics of saline- and HF-IHDF-treated patients at baseline

The baseline characteristics of the patients in the saline and HF-IHDF groups are shown in Table 1. Among all patients, the mean age was 78.8 ± 7.7 years in the saline group and 77.7 ± 7.6 years in the HF-IHDF group. There was no significant difference in the mean serum creatinine (sCRE) or estimated glomerular filtration rate (eGFR) between both the two groups (saline: 1.67 ± 0.19 mg/dl, 32.1 ± 3.8 ml/min/1.73 m², HF-IHDF: 1.74 ± 0.36 mg/dl, and 31.7 ± 7.0 ml/min/1.73m²). In the saline group, the proportion of patients with stage G3b chronic kidney disease (CKD) was significantly higher than in the HF-IHDF group (74.1% vs. 48.6%, \( p = .003 \)). The mean volume of the contrast medium used during the interventional procedure, the predicted risks for the occurrence of contrast-induced nephropathy (CIN) and for in-hospital hemodialysis (HD) were similar in the two groups.

#### 3.2 Time courses of sCRE and eGFR

Figure 3 shows the time courses of the sCRE and eGFR in the two groups. sCRE and eGFR were measured at three points in all patients:

| Variable                        | Saline (n = 54) | HF-IHDF (n = 76) | \( p \) value |
|---------------------------------|----------------|-----------------|-------------|
| Number of angiographical procedure (n, %) | CAG 25 (46.3) | 13 (17.1) | .0003 |
|                                 | PCI 22 (40.7) | 49 (64.5) | .006 |
|                                 | PPI 7 (13.0)  | 14 (18.4) | ns          |
| Age (years)                     | 78.8 ± 7.7    | 77.9 ± 7.4    | ns          |
| Male sex (n, %)                 | 39 (72.2)     | 61 (80.3)     | ns          |
| Hypertension (n, %)             | 30 (55.6)     | 57 (75.0)     | .016        |
| Diabetes mellitus (n, %)        | 28 (51.9)     | 45 (59.2)     | ns          |
| Chronic heart failure (n, %)    | 20 (37.0)     | 26 (34.2)     | ns          |
| Current smoker (n, %)           | 12 (22.2)     | 19 (25.0)     | ns          |
| LV-ejection fraction (%)        | 51.5 ± 16.1   | 51.1 ± 17.1   | ns          |
| HbA1c (%)                       | 6.4 ± 0.8     | 6.6 ± 0.7     | ns          |
| BNP (pg/ml)                     | 313.5 ± 215.8 | 334.4 ± 427.7 | ns          |
| Hemoglobin (g/dl)               | 11.5 ± 2.1    | 11.3 ± 1.7    | ns          |
| Serum creatinine (mg/dl)        | 1.67 ± 0.19   | 1.74 ± 0.36   | ns          |
| eGFR (ml/min/1.73m²)            | 32.1 ± 3.8    | 31.7 ± 7.0    | ns          |
| CKD stage                        | G3b 40 (74.1) | 37 (48.6)     | .003        |
|                                 | G4 14 (25.9)  | 39 (51.3)     | .003        |
| Medication (n, %)               | ACE-inhibitor 1 (1.9) | 10 (13.2) | .02 |
|                                 | ARB 26 (48.1) | 32 (42.1)     | ns          |
|                                 | Loop diuretic 19 (35.1) | 33 (43.4) | ns          |
|                                 | Mineralocorticoid receptor blockade 7(13.0) | 9 (11.8) | ns          |
| Volume of contrast media used (ml) | 116.8 ± 90.2 | 102.6 ± 58.2 | ns          |
| Predicted risk of CIN and in-hospital HD (n, %) | Moderate 12 (22.2) | 19 (25.0) | ns |
|                                 | Severe 31 (57.4) | 36 (47.3) | ns |
|                                 | Very severe 11 (20.4) | 21 (27.6) | ns |

Note: Predicted risk of CIN and in-hospital hemodialysis (HD) was calculated for each patient just after the interventional procedure using Mehran’s risk scoring. Moderate risk means the predicted risk of CIN and in-hospital HD are 14.0 and 0.12%, severe risk means those are 26.1 and 1.09%, and very severe risk means those are 57.3 and 12.6%. Values are presented as the means ± SEM.

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BMI, body mass index; BNP, brain natriuretic peptide; CAG, coronary angiography; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; LV, left ventricular; n, number; PCI, percutaneous coronary intervention; PPI, percutaneous peripheral intervention.

![FIGURE 3](image_url)  
Time course of renal function in the saline and HF-IHDF groups. Shown are serum creatinine (mg/dl) (a) and estimated GFR (ml/min/1.73 m²) (b) levels at baseline, day 2–3, 1 month, and 1 year after the interventional procedure. Values are presented as the means ± SE. Gray circles indicate the saline group and black circle indicate the HF-IHDF group.
at baseline and 2–3 days and 1 month after the interventional procedure. No significant difference was observed between the two groups at any of the 4 time points. After excluding patients who developed CIN or a need for HD, as well as those who were lost to follow up or who died during follow-up, data were measured from the remaining 37 patients in the saline group and 69 patients in the HF-IHDF group 1 year after the interventional procedure. In these patients, the sCr and eGFR values did not significantly differ at 1 year from the values measured at 2–3 days or at baseline in either group.

3.3 | Incidence of CIN

The predicted risk of CIN based on Mehran’s risk scoring and the actual incidence of CIN are shown in Figure 4a. The predicted risk of CIN was 29.5 ± 15.2% in the saline group and 31.7 ± 16.7% in the HF-IHDF group. However, 2–3 days after the interventional procedure, no patient with CIN was identified in the HF-IHDF group, though CIN was identified in 5 of 54 patients in saline group (9.3% vs. 0.0%, p < .05). The incidence of CIN 1 month after the interventional procedure was also significantly lower in the HF-IHDF group than the saline group (14.8% vs. 3.9%, p < .05).

To assess the effect of contrast dose on the occurrence of CIN, the patients in each group were divided into three subgroups (<2, 2–3, and > 3) based on the ratio of the contrast dose to the baseline eGFR (CV/eGFR ratio), after which the incidence of CIN was analyzed (Figure 4b). Two to three days after the interventional procedure, the CIN rate in all three subgroups was around 10% in the saline group (11.1%, 2 of 18 patients; 7.7%, 1 of 13 patients; 8.7%, 2 of 23 patients), whereas no patient experienced

**TABLE 2** Rate of requiring permanent HD within 1 year after the angiographical procedure

| Mean predicted risk of in-hospital HD based on Mehran’s risk scoring (%) |
|-----------------------------|-----------------------------|
| Saline group (n = 54)        | 3.2 ± 4.8                   |
| HF-IHDF-group (n = 76)       | 4.0 ± 5.3                   |

| Incidence of requiring permanent HD (n, %) |
|-----------------------------|-----------------------------|
| Saline group (n = 54)       | 0 (0)                       |
| HF-IHDF-group (n = 76)      | 0 (0)                       |

| Mean time up to permanent HD (days) |
|-----------------------------|-----------------------------|
| Saline group (n = 4)        | 94.0 ± 50.3                 |
| HF-IHDF-group (n = 2)       | 140.5 ± 48.8                |

| Cause of requiring permanent HD (n) |
|-----------------------------|-----------------------------|
| Saline group (n = 4)        |                            |
| Patient with CIN            | Increment of renal dysfunction 3   |
|                             | Infection 1                 |

Note: Predicted risk of the need for in-hospital hemodialysis (HD) calculated based on Mehran’s risk scoring, the actual frequency of permanent HD within 1 year after the interventional procedure, and the cause of permanent HD. Values of predicted risk of in-hospital HD and mean time up to permanent HD are presented as the means ± SE.
CIN in the HF-IHDF group. The CIN rate 1 month after the interventional procedure had increased in saline subgroups with CV/eGFR ratios of 2–3 (23.1%, 3 of 13 patients) or >3 (21.7%: 5 of 23 patients), while the incidence of CIN cases was much lower in the HF-IHDF group.

### 3.4 Rate at which permanent HD was required within 1 year after HF-IHDF

Based on Mehran's risk scoring, the predicted risk of in-hospital HD was 3.2 ± 4.8% in the saline group and 4.0 ± 5.3% in the HF-IHDF group; however, the actual incidences were 0% in both groups (Table 2). Moreover, our data indicate that during the 1 year of follow-up, 4 of 50 patients (8.0%) in the saline group and 2 of 73 patients (2.7%) in the HF-IHDF group required permanent HD. Among the patients with CIN 2–3 days after the interventional procedure, none required HD induction, whereas among patients who exhibited CIN 1 month after the interventional procedure 37.5% (3 of 8 patients) in the saline group and 66.7% (2 of 3 patients) in the HF-IHDF group required permanent HD. On the other hand, the fraction requiring HD among patients who did not develop CIN was quite low in both the saline group (2.8%, 1 of 36 patients) and HF-IHDF group (0%, 0 of 70 patients). In three of four patients in the saline group and one of two patients in the HF-IHDF group, the need for HD arose when patients who had developed CIN exhibited an increment in their renal dysfunction; infection was found in the others (Table 2).

### 3.5 One-year mortality

All-cause mortality within 1 year after the interventional procedure is summarized in Table 3. The overall 1-year mortality rate was 12.0% (6 of 50 patients) in saline group and 6.8% (5 of 73 patients) in the

### 3.6 In-hospital procedural complications

In-hospital procedural complications in the HF-IHDF group are shown in Table 4. Hemorrhage at the arterial puncture site was seen in two

#### TABLE 3 One-year mortality in saline- and HF-IHDF-group

| Variable | n (%) |
|----------|-------|
| Saline group (n = 50) | 6 (12.0) |
| HF-IHDF-group (n = 73) | 5 (6.8) |

#### TABLE 4 In-hospital complications after HF-IHDF

| Variable | n (%) |
|----------|-------|
| Myocardium infarction | 0 |
| Pulmonary edema | 0 |
| Hypotension during HF-IHDF | 0 |
| Hemorrhage at the puncture site | 2 (2.6) |
| Blood transfusion required | 1 (1.3) |
| Additional renal replacement therapy required | 0 |

Note: In-hospital complications among patients in the HF-IHDF group (n = 76).

*Low systolic blood pressure (<90 mmHg) necessitating catecholamine administration.

#### FIGURE 5 Scheme summarizing the long-term outcomes of the patients in this study. One-year follow-up of patients in the saline and HF-IHDF groups. (–) = negative, (+) = positive. CIN, contrast-induced nephropathy; HD, hemodialysis; PRD, progression of renal dysfunction fulfilling the definition of CIN from baseline to 1 year after the interventional procedure.
patients (2.6%) just after the interventional procedures, and one patient (1.3%) required a blood transfusion. No patients required additional renal replacement therapy, owing to decompensated congestive heart failure or acute renal failure.

3.7 | Summary of long-term follow-up after HF-IHDF

A summary of the 1-year follow-up is shown in Figure 5. The rate of progression of kidney dysfunction (PRD) among survivors who did not develop CIN at 2–3 days or 1 month after the interventional procedure, as well as the frequency of HD within the 1-year follow-up period, were significantly lower in the HF-IHDF group than the saline group (64.8%, 35/54 patients vs. 86.8%, 66/76 patients; p < .01). There were also more patients who died or required HD among those who newly developed CIN at 1 month than at 2–3 days after the interventional procedure in the two groups.

4 | DISCUSSION

It has been suggested that CIN occurs as a result of multiple mechanisms, including: (a) reduced renal blood flow due to a reduction in vasoconstrictors such as nitric oxide, prostaglandins I2 and E2, and an increase in such vasoconstrictive factors as endothelin and adenosine; (b) increased oxidative stress; (c) direct and immediate damage to tubular epithelial or mesangial cells. Numerous studies have addressed these issues, though hydration using 0.9% saline, which is thought to prevent CIN by maintaining renal blood flow, has only been established for the patients with normal kidney function. Indeed, given the high rate of CIN among patients treated with saline hydration alone (15–20%), especially among patients with advanced CKD (stage ≥3b), it appears that saline hydration alone is not sufficient to prevent CIN. In addition, although sodium bicarbonate hydration was expected to effectively prevent CIN in patients with advanced CKD through both maintenance of renal blood flow and suppression of oxidative stress, its superiority over saline hydration has yet to be clearly demonstrated.

HD was examined as renal replacement therapy with the idea of effectively removing contrast medium to prevent CIN. However, some studies could not verify a beneficial effect of HD. Marenzi et al. demonstrated that CHF performed for 4–8 hr before and 18–24 hr after PCI could prevent CIN in patients with stage G4 CKD to a greater degree than saline hydration. Because this result may be strongly influenced by the filtration of sCre itself, a second study by Marenzi et al. clarified that in patients with stage G4 to G5 CKD, significantly greater prevention of CIN was achieved with CHF performed for 6 hr before and 18–24 hr after PCI than with saline hydration. Notably, however, CHF performed only for 18–24 hr after PCI was not more effective than saline hydration. These results may indicate that CHF prevents CIN in patients with advanced CKD mainly through continuous administration of alkaline agents that reduce oxidative stress, not through removal of the contrast medium. However, the prolonged period of treatment is not realistic for patients.

The HF-IHDF described in the present study can remove contrast medium from the blood six times faster than standard CHDF, efficiently reducing renal damage from exposure by contrast medium. This enables the treatment time to be much shorter than with standard CHF. In our earlier studies of renal replacement therapy to prevent CIN, HF-IHDF was started just before each interventional procedure to achieve rapid and sustained removal of the contrast medium and was continued up to 2.5 hr after the procedure to eliminate the contrast medium remaining in the blood as quickly as possible. In addition, the levels of administered sodium bicarbonate are much higher with HF-IHDF than with the standard sodium bicarbonate hydration (105 mEq/hr vs. 9 mEq/hr). This high dose of sodium bicarbonate may not only reduce oxidative stress within the kidney but may also help to maintain fluid volume to avoid renal ischemia. Given these therapeutic effects, HF-IHDF has the potential to prevent CIN more effectively than other renal replacement therapies.

Hitinder et al. suggested that to reduce the likelihood of CIN, the contrast volume to creatinine clearance ratio (CV/CC ratio) should be kept below 3 in stage G3 CKD and below 2 in stage G4 CKD. In patients treated with HF-IHDF, the CIN rates 2–3 days and 1 month after the interventional procedure were lower than in the saline group, irrespective of the CV/CC ratio. This suggests HF-IHDF may increase the tolerance to contrast agents.

Because CIN is an acute kidney injury (AKI), it was difficult to know whether general criteria for CIN or the Acute Kidney Injury Network (AKIN) classification should be applied for diagnosis of CIN. According to the AKIN classification for patients with normal renal function, increased sCre within 48 hr or reduced urine output within 6 hr is diagnostic criteria for AKI. On the other hand, CIN is generally rare in patients with normal renal function, but its occurrence becomes more frequent as kidney function declines. In addition, patients with oliguria after the occurrence of CIN is also rare. Moreover, a change in sCre of 0.3 mg/dl, which is used for AKIN classification, appears to be too sensitive a diagnostic criterion for CIN in the patients with impaired renal function. For those reasons, we did not use AKIN classification for diagnosis of CIN. Moreover, diagnosis of CIN should generally be made 48–72 hr after contrast exposure, based on a >25% increase from the baseline sCre level or an increase of 0.5 mg/dl. However, a recent study suggested that 1 month after contrast exposure could be more important for long-term prognosis. This is because the 3-year survival rate among patients diagnosed with CIN at 1 month was markedly poorer than among those diagnosed with CIN at 48–72 hr. We therefore assessed the occurrence of CIN at both 2–3 days and 1 month after the interventional procedure. Consistent with that earlier finding, we observed that in both the saline and HF-IHDF group, the mortality rate and renal prognosis were poorer for patients who newly developed CIN at 1 month than for those who developed CIN at 2–3 days.

Because we found that the incidence of CIN was lower and kidney function was better preserved in HF-IHDF group than saline group during the 1 year of follow-up, we suggest that HF-IHDF may have the potential to improve long-term renal prognosis. Four patients in the saline group and two in the HF-IHDF group required permanent HD within the 1-year follow-up period, and both the 1-year mortality
rate and risk of permanent HD were higher among patients in both groups who developed CIN, which is consistent with earlier reports. Thus, the ability of HF-IHDF to reduce the incidence of CIN could contribute to improving the long-term prognosis of CKD patients undergoing procedures requiring administration of contrast medium.

5 | STUDY LIMITATIONS

Our study has two main limitations. First, our investigation was limited to a single center, and the number of the patients treated using HF-IHDF was small. A larger, multicenter, double-blind, randomized trial will be needed to confirm the effectiveness of HF-IHDF for preventing CIN in patients with advanced CKD. Second, our study was limited to patients receiving elective interventional procedures. An earlier report suggested that acute coronary syndrome is itself an independent risk factor for CIN due to the associated hemodynamic instability and hypoperfusion. Whether HF-IHDF has an ability to protect the kidneys in such an emergent state remains unclear.

6 | CONCLUSION

HF-IHDF during and after an interventional procedure requiring administration of contrast medium may have a potential to prevent CIN in patients with advanced CKD.

ACKNOWLEDGMENT

We would like to thank the members of our catheter laboratory, especially K. Shiota for collecting data and data analysis.

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How to cite this article: Oyamada N, Hamanaka I, Fujioka A, et al. Effectiveness of high flow-volume intermittent hemodiafiltration during and after intervention to prevent contrast-induced nephropathy in patients with advanced chronic kidney disease: A pilot study. Catheter Cardiovasc Interv. 2020;96:1174–1181. https://doi.org/10.1002/ccd.28640