Original Article

Catheter ablation for patients on hemodialysis with symptomatic atrial fibrillation

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Background: There are limited studies on the efficacy and safety of catheter ablation (CA) for patients with atrial fibrillation (AF) who receive intermittent hemodialysis (HD). This gap in the contemporary literature is notable as patients with AF receiving HD has higher incidence of AF and does not often tolerate medical management due to renal failure.

Methods: From Mar 2015 and Jan 2018, 25 consecutive patients on regular HD from two cardiac centers who underwent CA were retrospectively enrolled. Another 100 patients without HD or renal impairment, matched by age, sex, and AF type, were enrolled from these cardiac centers as the control group. All patients were followed up at month 3, 6, and every 6 months after the first CAs for 4 years, and 2.5 years after a second CA (if applicable), unless endpoints were reached. The primary endpoint was AF recurrence after CA, and the secondary endpoints included symptomatic AF and all-cause mortality during the follow-up period.

Results: AF patients receiving intermittent HD had a higher prevalence of hypertension (P=0.005), and heart failure (P=0.041). During the mean follow-up period of 37.6±17.4 months after the first CA, 14 out of the 25 HD patients (56.0%) remained free from AF recurrence, compared with 77 in the control patients (77.0%; P=0.021). Twenty (80.0%) patients in the HD group did not experience symptomatic AF. Second CAs were performed on 5 HD patients and 11 control patients, consequently 4 out of 5 (80.0%) HD patients and 7 out of 11 (63.6%) control patients had no AF recurrence (P=0.626) within 21.1±12.0 months after the second CA. Tamponade was the only procedural complication documented in both groups. All-cause mortality was higher in the HD group (log-rank P=0.004); however, the observed mortality was not related to AF recurrence.

Conclusions: CA is a potential efficacious and safe treatment of AF for HD patients. The AF recurrence rate is higher after a single ablation compared with the general population, but multiple ablations seem to improve outcomes for HD patients.

Keywords: Atrial fibrillation (AF); catheter ablation (CA); hemodialysis (HD)

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Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia in the general population, and it is becoming an increasingly common condition among patients with end-stage renal disease (ESRD) (1). Patients with ESRD are at higher risk of developing AF. Studies have shown that AF prevalence in ESRD patients is 15–40%, 2- to 3-fold higher than the general population (2-4). AF increases mortality by 1.72-fold and the incidence of ischemic stroke by 9.8-fold among ESRD patients receiving intermittent hemodialysis (HD) (5). In clinical practice, once acute AF attack occurs during a HD session, patients are usually too symptomatic to continue HD sessions; and if AF-related hypotension or hemodynamic instability develops, dialysis sessions must stop completely (6). The interruption of HD leaves ESRD patients undertreated, therefore a reliable treatment for AF is needed to improve the quality of life for patients requiring chronic HD.

Rate control and rhythm control are among the first-line therapies for patients with AF (7,8). The antiarrhythmic drugs (AADs) are normally considered first for rate and rhythm control, besides anticoagulation. However, AADs are mainly cleared renal, thus AAD usage is largely restricted in ESRD patients. Even if the AADs can be administered, efficacy among ESRD patients is unpredictable. Researchers have previously reported that rhythm control with catheter ablation (CA) provides superior sinus rhythm maintenance and symptom improvement in the general population (9-12). As a consequence of these findings, CA is now widely utilized in treatment of AF when medications are unable to yield adequate symptom control or when patients cannot tolerate medical therapy (8,13). While the safety and efficacy of CA to restore and maintain sinus rhythm have been established in the general population (14), most of the large-scale AF studies have excluded patients receiving HD. Theoretically, it is reasonable to predict that CA can be an option for HD patients with symptomatic AF. However, there are only limited published data and clinical experience in this specific population. It is therefore important to further confirm whether CA is safe and effective in managing AF among HD patients.

In this study, we reviewed the clinical data collected from two cardiac centers in China to provide analysis of the efficacy and safety of CA for AF among HD patients, including all-cause mortality after CA. We present the following article in accordance with the STORBE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-410/rc).

Methods

Study population

We retrospectively identified 25 consecutive patients on regular HD who for the first time received CAs for drug refractory symptomatic paroxysmal or persistent AF at two cardiac centers in China between Mar 2015 and Jan 2018. During the same period, another 100 (ratio of 1:4) patients with matched age, gender, and AF type were enrolled in the control group. Control subjects received their first CA for drug refractory AF, but did not have ESRD or renal impairment. The exclusion criteria included patients who had structural heart diseases such as congenital heart disease, valvular heart disease, dilated cardiomyopathy, hypertrophic cardiomyopathy and myocardial infarction, or transient AF caused by reversible cause (e.g., cardiac surgery, pulmonary embolism, untreated thyroid disease). Both transthoracic and transesophageal echocardiography were performed in all the participants to exclude left atrial thrombosis before the ablation procedure.

The study complied with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Beijing Friendship Hospital (No. 2022-P2-130-01) and the Institutional Review Board of Beijing Anzhen Hospital (No. D11110700300000). The individual consent for this retrospective analysis was waived.

Vascular access

Vascular access was routinely obtained from the right femoral vein using the traditional method by palpating the femoral artery pulse as a landmark and puncturing medially in the direction of the navel until reflux of venous blood. Two sheaths were used, one for a deflectable decapolar catheter positioned in the coronary sinus, and the other one for an ablation catheter (ThermoCool SmartTouch, Biosense-Wbster, Diamond Bar, CA, USA) advanced to the left atrium after a single successful transseptal puncture. After the procedure, sheaths were removed and manual compression was applied at the venous access site for 3–5 min or until no bleeding observed. Any rebleeding was treated by manual compression for a further 3–5 min or until no bleeding observed. No venous closure or sutures were applied.

CA

All AADs were discontinued at least 5 half-lives prior to

ablation, except for amiodarone which was stopped at least 1 month before the procedure due to its very long half-life time. All participants underwent radiofrequency CA. In these two cardiac centers, the CA was performed on all participants in the same way as the procedure guideline describes (14). The procedures were guided by a 3D mapping system (CARTO 3; Biosense-Webster, Diamond Bar). For paroxysmal AF, bilateral circumferential pulmonary vein isolation (CPVI) was performed to completely isolate all pulmonary veins (PVs). Additional liner ablations at the left atrial roof (LAF), mitral isthmus (MI), or cavotricuspid isthmus (CTI) were performed if the AF could not be terminated by PV isolation. For persistent AF, in addition to CPVI, liner ablation at LAF, MI, and CTI were required. If the patient did not convert to sinus rhythm after ablation, cardioversion was conducted to convert AF to sinus rhythm. At the discretion of the operator, additional ablations of the non-PV foci, superior vena cava (SVC), or complex fractionated atrial electrograms (CFAEs) were performed (15,16). The procedural end point was the achievement of CPVI and bidirectional conduction block of each ablation line.

For the patients who had AF recurrence and needed a second ablation, the PVs were checked for reconnections and each ablation line was checked for conduction recovery (if performed in first procedure). The second ablation end point was complete CPVI and linear bidirectional block without inducibility of atrial tachyarrhythmias by burst pacing (16). After the ablation procedure, routine electrocardiogram (ECG) monitor was performed on all patients for 6 h.

Follow-up

The trial was designed to follow the participants for four years after the first CA. For those who underwent a second CA, a 2.5-year follow-up period was intended after the procedures. After CA, a type I or III AAD was prescribed for all patients for 3 months. An oral anticoagulation (OAC) was also given for only 3 months if the CHA_2DS_2-VASc score was lower than 2. If AF recurred, patients resumed OACs and AADs.

All the patients were followed up at month 3, and 6 after CAs and then every 6 months, either by telephone interviews or an in-person clinic visit; 12-lead ECGs and a 24-h Holter monitoring were prescribed for each follow-up. Additional ECGs were ordered if arrhythmic symptoms occurred. Successful ablation was defined as the absence of any AF lasting for at least 30 s, without any AAD after the post-ablation blanking period of 3 months (17).

Endpoints

The primary endpoint was AF recurrence after the 3-month post-ablation blanking period during the follow-up. The secondary endpoints included symptomatic AF and all-cause mortality during the follow-up period. The incidence of periprocedural complications was recorded, such as cardiac tamponade, stroke/transient ischemic attack (TIA), vascular complications, and hemorrhage from index procedure through 90 days following the procedure. Periprocedural complications were assessed as follows: prior to discharge, patients were examined for procedural complications; following discharge, patients were advised to contact their study coordinator if they experienced any complications; at the month 3 follow-up visit, patients were asked about any procedural complications.

Statistical analysis

Student's *t*-test and Wilcoxon rank-sum test were used for normally distributed continuous and non-normally distributed continuous variables, respectively, in the formats of mean ± standard deviation (SD) median (25th–75th percentile). Categorical variables were analyzed by using χ^2 test or Fisher's exact. To reduce potential confounding and to adjust for differences in baseline characteristics between the HD patients and control patients, a 1:4 matching was performed. Kaplan-Meier analysis and log-rank test were applied to compare the cumulative AF-free rates of two groups. P values were calculated based on 2-sided tests, with $P<0.05$ deemed statistically significant. STATA 13.0 was used for statistical analysis (Stata Corp., College Station, TX, USA).

Results

Baseline characteristics

The 25 AF patients with HD and the 100 AF patients that did not require HD were compared as intervention and control groups. The baseline characteristics were summarized in *Table 1*. The two groups had no difference in age, gender, body mass index (BMI), medical history (diabetes, hypertension, coronary artery disease, and stroke/TIA), AF type, AF duration, and echocardiographic

Table 1 Baseline patient characteristics

Variables	HD (–) (n=100)	HD (+) (n=25)	P value
Age (years), mean ± SD	59.7±5.2	58.1±9.2	0.257
Male, n (%)	67 (67.0)	16 (64.0)	0.776
BMI (kg/m^2), mean ± SD	25.5±3.2	25.0±3.2	0.497
Duration of AF (months), median (25th–75th percentile)	24.0 (6.5–60.0)	12.0 (6–24.0)	0.165
PAF, n (%)	90 (90.0)	23 (92.0)	0.761
Persistent AF, n (%)	10 (10.0)	2 (8.0)	0.761
Smoke, n (%)	47 (47.0)	9 (36.0)	0.323
Drink, n (%)	36 (36.0)	4 (16.0)	0.055
Hypertension, n (%)	68 (68.0)	24 (96.0)	0.005
Diabetes, n (%)	24 (24.0)	6 (24.0)	1.000
Coronary artery disease, n (%)	19 (19.0)	4 (16.0)	0.729
Stroke/TIA, n (%)	7 (7.0)	3 (12.0)	0.410
Heart failure, n (%)	1 (1.0)	2 (8.0)	0.041
LAD (mm), mean ± SD	38.7±5.0	40.3±9.2	0.254
LVEDD (mm), mean ± SD	48.7±4.3	48.3±9.9	0.743
LVEF (%), mean ± SD	64.2±5.5	61.6±6.1	0.041
EHRA classification, n (%)			
EHRA II	17 (17.0)	2 (8.0)	
EHRA III	77 (77.0)	21 (84.0)	
EHRA IV	6 (6.0)	2 (8.0)	
Duration of HD (years), mean ± SD	–	6.7±4.1	
Cause of kidney disease			
Chronic glomerulonephritis (n)	–	13	
Polycystic kidney disease (n)	–	2	
Drug-induced renal damage (n)	–	2	
IgA nephropathy (n)	–	1	
Nephrotic syndrome (n)	–	1	
Diabetes (n)	–	3	
Hypertension (n)	–	3	

HD, hemodialysis; SD, standard deviation; BMI, body mass index; AF, atrial fibrillation; PAF, paroxysmal atrial fibrillation; TIA, transient ischemic attack; LAD, left atrium diameter; LVEDD, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; EHRA, European Heart Rhythm Association.

parameters such as left atrial diameter (LAD) or left ventricular end-diastolic diameter (LVEDD). HD patients tended to have higher prevalence in hypertension and heart failure compared with the control group. The detailed causes of kidney disease and HD duration are also shown in *Table 1*.

Outcomes after the first CA

The details of the first ablation and periprocedural complications are listed in *Tables 2,3*. There was no difference in CA procedure strategy between the two

Table 2 Procedural strategy of the first and second ablation

Procedural profile	HD (–)	HD (+)	P value
First ablation, n/N (%)			
CPVI	100/100 (100.0)	25/25 (100.0)	–
CTI	34/100 (34.0)	6/25 (24.0)	0.338
SVCI	11/100 (11.0)	1/25 (4.0)	0.288
Other lines	18/100 (18.0)	4/25 (16.0)	0.814
Second ablation, n/N (%)			
CPVI	11/11 (100.0)	5/5 (100.0)	–
CTI	5/11 (45.5)	2/5 (40.0)	0.838
SVCI	2/11 (18.2)	0	0.308
Other lines	4/11 (36.4)	1/5 (20.0)	0.513

HD, hemodialysis; CPVI, circumferential pulmonary vein isolation; CTI, cavo-tricuspid isthmus; SVCI, superior vein cava isolation.

Table 3 Incidence of periprocedural complications associated with ablation

Procedural profile	HD (–)	HD (+)
First ablation (n)	100	25
Cardiac tamponade	1	1
Stroke/TIA	0	0
Hemorrhage	0	0
Vascular complications	0	0
Second ablation (n)	11	5
Cardiac tamponade	0	0
Stroke/TIA	0	0
Hemorrhage	0	0
Vascular complications	0	0

HD, hemodialysis; TIA, transient ischemic attack.

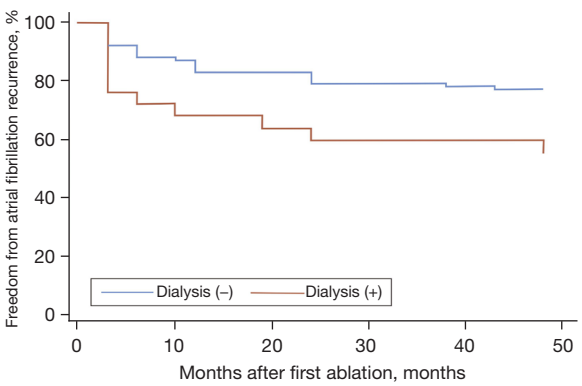

Figure 1 Kaplan-Meier analysis of the time to recurrent AF after the first CA procedure (log rank P=0.021). AF, atrial fibrillation; CA, catheter ablation.

groups. One cardiac tamponade event during the procedure was documented in each group with a P value of 0.285. There was no other periprocedural complications such as stroke/TIA, hemorrhage, or other vascular complications in either group; 14 of 25 patients on HD and 77 of 100 patients in the control group remained free from AF recurrence after the first CA during mean follow-up period of 37.6±17.4 months. The HD patient group had a higher recurrence rate compared to the control group (log-rank P=0.021), as shown in *Figure 1*. Twenty (80.0%) of the HD patients remained free from symptomatic AF during the mean follow-up of 37.6±17.4 months; 5 out of the 11 HD patients (45.5%) who had recurrent AF, underwent the second CAs because of intolerable AF symptoms; the other 6 (54.5%) were asymptomatic and did not require AADs nor additional CAs.

Outcomes after the second CA

The details of the second ablation and periprocedural complications are summarized in *Tables 2,3*. As mentioned above, 5 out of 11 (45.5%) HD patients with AF recurrence had received a second CA. In the control group, 11 out of 23 (47.8%) patients with AF recurrence received a second CA. PVs reconnection was noted and ablated

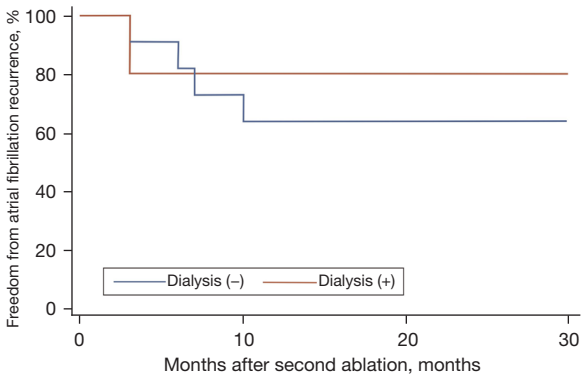

Figure 2 Kaplan-Meier analysis of the time to recurrent AF after the second CA procedure (log rank P=0.626). AF, atrial fibrillation; CA, catheter ablation.

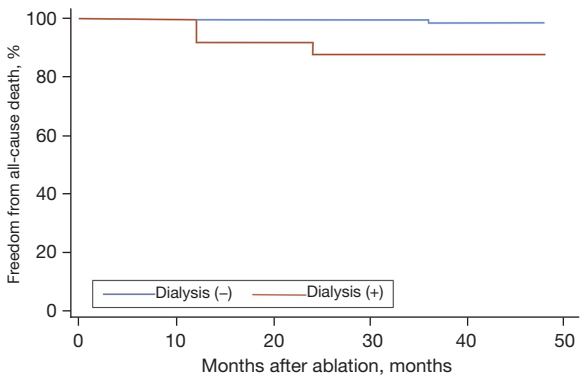

Figure 3 Kaplan-Meier analysis of the time to all-cause death after CA (log rank P=0.004). CA, catheter ablation.

during the second CA in all of the 16 patients. No periprocedural complications were documented. Among those who had second CAs, 4 (80.0%) from the HD patient group and 7 (63.6%) from the control group remained in sinus rhythm within a mean follow-up period of 21.1±12.0 months after the second CAs. No difference was found in the AF recurrence rates between the two groups (log-rank P=0.626), as shown in *Figure 2*; 4 out of 5 (80.0%) HD patients who received second CAs remained free from symptomatic AF during the mean follow-up period of 21.1±12.0 months.

All-cause mortality after the CA

During the mean follow-up of 37.6±17.4 months, 3 (12.0%) of the 25 HD patients had died. One of them had AF recurrence and died from an accident. The other two patients died of malignancy and severe systematic infection. None of these patients suffered from heart failure or stroke that related to recurrent AF; 1 (1.0%) of the 100 patients from the control group died without AF recurrence due to systematic infection. Mortality was higher in the HD patient group (log-rank P=0.004), although not related to AF recurrence (*Figure 3*).

Discussion

In this study, we examined utilization of CA for symptomatic AF patients on HD. We found that: (I) after the first ablation, although AF recurred more often in the HD patient group, there were still 56.0% of patients with sinus rhythm in the absence of any AADs during the mean follow-up of 37.6±17.4 months; (II) after a second ablation for AF recurrence, 80.0% of patients in the HD group successfully achieved sinus rhythm during the mean follow-up of 21.1±12.0 months, which is similar to the non-HD group, and HD patients showed PV reconnection during the second ablation; (III) CA may be safe in HD patients; (IV) ~80.0% HD patients remained free from symptomatic AF during follow-up.

AF is prevalent in ESRD patients and negatively impacts patient outcomes (1,4). In the general population, patients with comorbidities such as advanced age, hypertension, and pre-existing cardiovascular disease are at higher risk of developing AF. Since these risk factors are commonly seen in the ESRD population, it is not surprising that a higher prevalence of AF is seen in this group of patients. In ESRD patients receiving routine HD, AF occurs significantly more often on a dialysis day and even during HD, likely due to rapid volume change and electrolyte shifts (6). The sudden ventricular rate increase due to AF can cause patient complaints of palpitation or even hemodynamic instability during dialysis for which HD session must cease. Sinus rhythm maintenance is beneficial in reducing uncomfortable symptoms, and therefore adequate ESRD management.

Studies have confirmed the benefits of CA on maintaining sinus rhythm and improving AF-related symptoms in the general population (9,10). However, the effectiveness of CA in AF patients on HD remains unclear. Sairaku *et al.* (18) reported 54% of HD patients were free from AF recurrence after an initial ablation, versus 78% in control group. Further, 67% of HD patients versus 88% of the patients from control group maintained sinus rhythm after a second ablation, with no life-threatening complications noticed. Another study by Takigawa *et al.* (19)

showed that although AF recurred more frequently in HD patients than non-HD patients (P<0.0001) after multiple CAs, there were still ~50% patients in the HD group that remained in sinus rhythm and there was no significant difference in complications between the HD and control groups. These findings indicated that CA is effective in HD patients, but that the rate of AF recurrence is higher in HD patients compared with control patients. Despite these challenges in the baseline characteristics of HD patients, still more than half of patients could maintain sinus rhythm after multiple CAs.

The general identified risk factors for AF recurrence after CA included hypertension, heart failure, left atrial enlargement and renal dysfunction that were also seen in present HD patients (12). Besides, the non-physiological nature of HD and long-term dialysis causes atrial structural changes that may predispose patients to higher AF recurrence rate following ablation (4). In the present study, the AF recurrence-free rate after the second ablation was similar in both groups, which was consistent with a study by Hayashi *et al.* (20). Our study did not show any superior outcome after a single session of CA in treating AF among HD patients, whereas a strategy involving multiple CA sessions was favorable. This result is encouraging, considering the higher risks of AF in HD patients than non-HD patients. However, it should be interpreted with caution. Only a small number of patients received a second CA in our study, and the mean follow-up time was only 21.1±12.0 months. As long as patients continue receiving chronic HD, further atrial structural change will be inevitable and therefore potential AF will be likely to develop. Even multiple CAs may not terminate AF completely. Further long-term studies to assess sustained efficacy of CA are needed to confirm our findings. Nonetheless, during the second ablations, we found that patients with recurrent AF in both groups had a reconnection of the PVs and 80% of HD patients remained AF-free. One might infer that HD patients may have foci within the PVs triggering AF, similar to the situation in the general population, a finding that is consistent with previous reports (18,20). One study suggested that because of the difficulty in achieving complete elimination of transmural lesions of PVs, three or more CA sessions may be needed to improve outcomes (19). Complete CPVI is vital. It is though not clear if cryo-balloon ablation or thermal balloon ablation leads to a lower incidence of AF recurrence (21). Further studies focusing on the maintaining sinus rhythm and the effectiveness of different types of CA for this population is warranted.

Regarding a safety profile, our result was consistent with previous findings that HD patients did not experience more periprocedural complications from CA procedures compared with control group (18-20). A more recent study showed that patients with chronic kidney disease (CKD)/ESRD undergoing AF ablation were associated with higher bleeding complications, but in-hospital mortality, vascular complications, cardiac tamponade complications and neurological complications were not significantly different compared with non-CKD patients (22). Higher bleeding complications in CKD patients might be part due to older age (72.9±10.7 years old) and combined with more comorbidities as compared with our study; however, it is unclear whether the bleeding complications were ablation procedure related. Additionally, considering a high proportion of ESRD patients had underlying coagulopathy, this might have also contributed to bleeding risk (23). Therefore, whether CA is totally safe in ESRD/HD patients with AF warrants additional investigation, with particular focus on careful preoperative assessment in this high-risk population.

Additionally, our study showed about 80.0% of HD patients remained asymptomatic either with AF recurrence or free from any AF recurrence after CA during follow-ups. Although the rate of AF recurrence is high, patients' complaints of palpitation were reduced in presents HD patients, which theoretically would have improved the adherence to HD therapy. However further exploration and analysis are needed to confirm this hypothesis.

The mortality rate is high in regular dialysis patients, and it was about 9% per year according to the Japanese Society for Dialysis Therapy (24). Additionally, reports showed that AF in dialysis patients was associated with a higher mortality rate (2,5,25). In the present study, all-cause mortality after CA was significantly higher among HD patients (12.0%) compared to control group (1.0%). However, none of the deaths were directly related to AF burden. Whether AF CA in HD patients is associated with mortality change remains unclear, and further studies with larger sample sizes are needed to elucidate this potential relationship.

Study limitations

Our study had a few limitations as it was a retrospective study with a small sample size and limited power. While the study did not aim to clarify the mechanisms of initial or recurring AF among HD patients, we did identify PV gap

as one of the potential contributing mechanisms. Lastly, it is possible that AF recurrence was underestimated since the study only recorded ECGs or 24 h Holter during the follow-up visits and it is possible that patients may have had temporary asymptomatic AF events between scheduled follow-up visits.

Conclusions

In conclusion, considering that AADs are largely restricted in ESRD patients receiving HD, CA may be a feasible option to treat AF in HD patients. Our data suggest that although AF recurrence after first ablation can be common, a second ablation can lead to a favorable result. CA may be safe in HD patients. Larger sized studies are required to confirm the benefits, potential effects on mortality related to AF recurrence, and the long-term prognosis of CA among HD patients.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-410/rc

Data Sharing Statement: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-410/dss

Peer Review File: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-410/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-410/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Beijing Friendship Hospital (No. 2022-P2-130-01) and the Institutional Review Board of Beijing Anzhen Hospital (No. D11110700300000). The individual patient written consent for this retrospective analysis was waived in the current study.

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