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Current apparent treatment-resistant hypertension in patients undergoing peritoneal dialysis: A multi-center cross-sectional study

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Abstract

Apparent treatment-resistant hypertension (aTRH) is the most commonly used term to report resistant hypertension (RH) and is considered as a common problem in dialysis population. However, few reports have focused on peritoneal dialysis (PD) hypertensive patients. The authors conducted a multi-center cross-sectional study involving 1789 PD patients from nine centers in Guangdong, China. The prevalence of aTRH was estimated by home blood pressure (BP) monitoring. Evaluating drug adherence through Eight-item Morisky Medication Adherence Scale (MMAS-8) and pill counting was performed to assess RH in one PD center. Related factors of aTRH were analyzed using logistic regression analysis. The prevalence of aTRH in PD patients was estimated at 42.2% (755 out of 1789 hypertensive patients) based on home BP. Of

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those, 91.4% patients were classified as uncontrolled RH, 2.0% as controlled RH, and 6.6% as refractory hypertension. The prevalence of RH was 40.6% and 41.9% among those with medium/high adherence based on the MMAS-8 scores and the pill counting rate, respectively. PD patients who were younger, with higher body mass index, with lower serum albumin and poorer dialysis adequacy were significantly associated with higher aTRH incident. In conclusion, the present study demonstrates a high prevalence of aTRH in PD population, which occurs in about two in five treated hypertensive patients. Nutritional status and dialysis adequacy might tightly associate with aTRH.

KEYWORDS
apparent treatment-resistant hypertension, dialysis adequacy, home blood pressure monitoring, peritoneal dialysis

1 | INTRODUCTION

Hypertension is a most common complication in end staged renal disease (ESRD) patients undergoing dialysis with the prevalence about 90%, and is notoriously difficult to control.[1–4] Resistant hypertension (RH), also called difficult-to-treat hypertension, is generally defined as failure to control blood pressure (BP) concurrently using at least three anti-hypertensive drugs, or hypertension controlled by at least four medications.[5] This definition represents a heterogeneous patient group, including those with uncontrolled or controlled BP, pseudo-resistance (e.g., white-coat hypertension, inaccurate BP measurements, or elevated BP because of non-adherence to drugs), and refractory hypertension (RfH) (uncontrolled BP with at least five anti-hypertensive medication classes).[5,6] Given the potential pseudo-resistance, apparent treatment-resistant hypertension (aTRH) is still the most commonly used term in clinic and in many studies.[7–10] Research of aTRH has been fully evaluated with the prevalence of 0.5%–14.3% in general hypertensive population, and 1.6%–42% in predialysis chronic kidney disease (CKD) patients.[7,11–13] Absolutely, it was associated with a greater risk of cardiovascular events and progression of renal failure.[8,12,13] In two studies from hemodialysis (HD) patients, the prevalence seemed to be similar (18%–24%) compared to those on predialysis CKD population.[1,14] Nevertheless, research focused on peritoneal dialysis (PD) population is lacking.

It is up to approximately 300, 000 patients receiving PD in the world, and this number is greatly increasing in many countries, especially in Southeast Asia and China.[15,16] Although PD is regarded as a continuous renal replacement modality, patients are prone to suffer from water-sodium retention because of inefficient transportation and peritoneal injury, which might be a central feature of RH.[16,17] Besides, diuretic agents might not be generally used due to the lack of residual renal function.[18,19] Thus, the aTRH should be distinctive in this population. In order to estimate the current aTRH prevalence in PD population, we conducted a multi-center cross-sectional study including 1789 PD hypertensive patients from nine centers.

2 | MATERIALS AND METHODS

2.1 | Study population

This was a multi-center, cross-sectional study approved by nine PD centers from five tertiary hospitals and four secondary hospitals in Guangdong Province, China, from December 1st 2019 to March 31st 2021. All the participants evaluated and enrolled in the outpatient department or follow-up center of PD have provided written informed consent (ethics number NFEC-2019-191, approved by the Research Ethics Committee of Nanfang Hospital). Patients undergoing PD more than 1 month and aged 18 years or older were eligible for this study. Patients who were not willing to join the study, unable to complete home BP monitoring, using non-steroidal anti-inflammatory drugs (NSAIDs), treated with PD and HD simultaneously, or with secondary hypertension, such as renovascular disease, adrenal disorders, Cushing syndrome, aortic coarctation during the study period were excluded.

2.2 | Definitions

Definitions of hypertension, aTRH, uncontrolled RH, controlled RH, and RfH were based on home BP. Hypertension was defined as BP at least 130/80 mmHg or being on treatment with any anti-hypertensive drugs.[20] ATRH was defined as uncontrolled BP (systolic BP [SBP] ≥130 mmHg and/or diastolic BP [DBP] ≥80 mmHg) with concurrent use of at least three anti-hypertensive medications of different classes, or BP controlled by at least four medications according to the American College of Cardiology/American Heart Association (ACC/AHA) guideline.[20] The use of diuretics was recorded but these drugs were not counted as a class of anti-hypertensive medication because of the limited effectiveness in dialysis patients.[18,19] Moreover, uncontrolled RH (BP ≥ 130/80 mmHg with three or four medications), controlled RH (BP < 130/80 mmHg with at least four medications), and RfH (BP ≥ 130/80 mmHg with at least five medications) were also defined according to the ACC/AHA guideline.[20] Threshold of 140/90 mmHg based on office BP was also used to define aTRH according to the

European Cardiovascular and Renal Medicine (EURECA-m) consensus.[21] Urine volumes less than 100 ml/d in patients were defined as the loss of residual renal function (RRF).[22]

2.3 | Blood pressure monitoring

Home and office BP were measured according to the ACC/AHA guidelines.[20] Briefly, office BP was measured using the validated Omron oscillometric BP monitors and home BP monitors were also appropriately calibrated by validated BP monitors.[23] Patients were advised to refrain from smoking, caffeinated beverages, alcohol intake, or exercise within 30 min, ensure at least 5 min of quiet rest before BP measurements, and then measured in a separate space without doctors or nurses. Correct sitting of patients were educated, which included sitting with back supported on chair and feet on floor, and keeping arm supported on table with the upper arm at heart level. During the rest period or during the measurement, conversation was avoided. Three BP readings were taken 1–2 min apart. The first BP reading was deleted and the average of the second and third BP reading was taken in the analysis. If left/right inter-arm differences were significant, the patients were instructed to measure BP in the arm with higher readings.[20] For home BP monitoring, patients were also trained in equipment selection, device application, and BP readings record. Automatic BP monitor devices were used by patients for home BP measurements. Patients were also required to have rest and sit correctly as mentioned above, and were asked to take three readings 1–2 min apart in morning before taking medications and in evening before supper for three consecutive days. There were three BP readings for each measurement, the first BP reading was removed, and the second and third readings were averaged from the three consecutive days for analysis.

2.4 | Data acquisition

Data and information including age, sex, body mass index (BMI), presence of diabetes mellitus, cigarette smoking and alcohol intake, anti-hypertension medications intake, PD vintage, dialysis modality, ultrafiltrated (UF) volume, and urine volume were obtained from the questionnaires (Figure S1) when patients came for outpatient clinic visit. The closest PD characteristics (dialysate glucose concentration [GLUC], weekly total Kt/V and peritoneal equilibration test [PET] types), laboratory examinations (serum creatinine, serum albumin, and blood hemoglobin), erythropoiesis-stimulating agents (ESA) dosage, other drugs contributing to BP (NSAIDs, antidepressants, atypical antipsychotics, decongestants, immunosuppressants, oral contraceptives, systemic corticosteroids, and angiogenesis inhibitors) and presence of secondary causes of hypertension were obtained from the medical records. The classes of anti-hypertensive drug included angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), calcium channel blockers (CCB), beta-blockers, alpha-blockers, and others (including centrally acting alpha-agonists, direct renin inhibitors, vasodilators and traditional Chinese medicine for treating hypertension). All anti-hypertensive medications were prescribed by physicians according to CKD guideline.[24]

Conventional weekly total Kt/V, and PET types were measured by standard methods.[25,26] We quantified dialysate glucose concentration formula as follows:

Dialysate glucose concentration (%) = Σ (glucose concentration × input volume)/total input volume. For example, if a patient is treated by continuous ambulatory peritoneal dialysis (CAPD) with 1.5% dialysate twice per day + 2.5% dialysate twice per day, the glucose concentration = (1.5% × 2L × 2 + 2.5% × 2L × 2)/8L = 2.0%.

2.5 | Adherence of anti-hypertensive treatment

We also evaluated the drug adherence by Eight-item Morisky Medication Adherence Scale (MMAS-8) and pill counting in one PD center. MMAS-8 is a structured, self-reported measure of medication adherence, and was validated in Chinese language.[27] The scale consists of seven yes/no items and one five-point scale to measure specific behavior about medication adherence (Figure S2). Patients with MMAS-8 scores ≥6 and <6 were classified into medium/high adherent and low adherent, respectively. Pill counting was performed between two clinic visits with a standard process.[28] Adherence rate was calculated as (the number of pills that should be left)/(the actual number of pills left) × 100%. The rate ≥80% and <80% was regarded as high adherence and low adherent, respectively.

2.6 | Statistical analyses

Stata 17.0 software was used for the statistical analyses. The *t*-test, Kruskal-Wallis test, or chi-squared test was used to compare continuous or categorical variables for baseline characteristics with or without aTRH. Un-adjusted and adjusted logistic regression analyses were performed to evaluate the association of aTRH with clinical characteristics. Demographic characteristics (age, sex, BMI, diabetes, smoker, and drinker), dialysis indicators (PD vintage, RRF, UF volume, dialysate glucose, and Kt/V), biochemical examinations (serum creatinine, serum albumin, and blood hemoglobin) and ESA dosage were included in adjusted logistic regression analysis. The continuous data were shown as the mean ± standard difference (SD) or median (interquartile range [IQR]), the categorical data were shown as number (proportion), and the odd ratio (OR) data were shown as OR (95% CI). A $P < 0.05$ was considered to be statistically significant.

3 | RESULTS

3.1 | Population description and apparent treatment-resistant hypertension prevalence based on home blood pressure

There were totally 2181 PD patients involved in this cross-sectional study. After excluding those with secondary hypertension (14 patients),

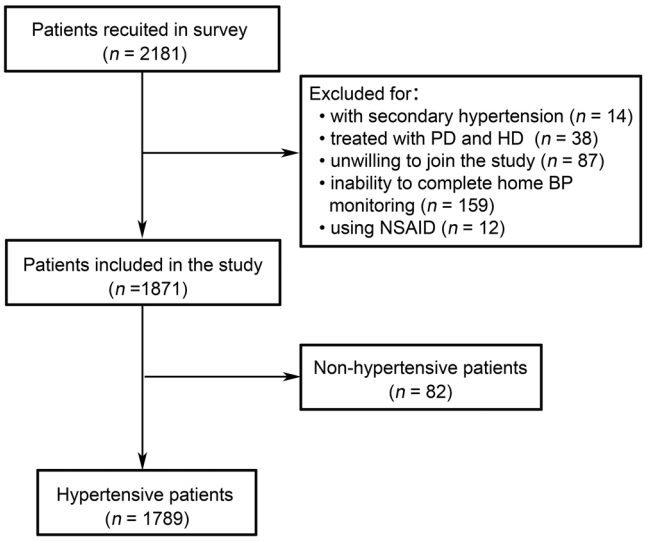

FIGURE 1 Flow chart of the study population. PD, peritoneal dialysis; HD, hemodialysis; BP, blood pressure; NSAIDs, non-steroidal anti-inflammatory drugs

treated with PD and HD simultaneously (38 patients), not willing to join the study (87 patients), inability to complete home BP monitoring (159 patients), or using NSAIDs (12 patients), 1871 patients were enrolled in this study (Figure 1). Of these 1871 patients, 1789 (95.6%) had hypertension (1653 were defined by receiving antihypertensive drug criterion, and 136 by BP more than 130/80 mmHg criterion). The aTRH prevalence among PD hypertensive patients was 42.2% (755/1789), including uncontrolled RH (91.4%, 690/755), controlled RH (2.0%, 15/755), and RfH (6.6%, 50/755) (Figure 2). The prevalence of aTRH was similar in different hospital grades (43.1% from tertiary hospital vs. 40.5% from secondary hospital, $P = 0.283$, Table S1) and in different centers (Figure S3).

The clinical characteristics of PD hypertensive patients with or without aTRH were summarized in Table 1. Of them, the mean age was 49.8 ± 13.5 years old, 53.0% were male, 19.3% were presence of diabetes mellitus, 17.0% were smokers, 9.1% were drinkers, the median PD vintage was 26 (11–50) months, and most patients received CAPD (96.4%). About 1490 (79.6%) patients have received erythropoietin, the median ESA dosage was 7000 (2500–10, 000) units per week. Patients with aTRH were younger, with higher BMI, had lower serum albumin, and had poorer dialysis adequacy.

3.2 | Distribution of anti-hypertensive drugs

We next analyzed the distribution of anti-hypertensive drugs being applied in the whole PD population. As shown in Figure 3A, classes of anti-hypertensive drug ranged from 0 to 6 (median: 2, IQR: 1-3). These medication classes included CCB (77.7%), ARB (53.2%), beta-blockers (50.2%), alpha-blockers (31.3%), ACEI (9.4%), and others (1.5%) (Figure 3B). The detailed use of anti-hypertensive medication classes of patients with or without aTRH was shown in Figure 3B. Approximately 96.1% of the aTRH patients received CCB medication, and the next most frequently class was beta-blocker. As shown in Table S2, the total number of tablets were 4 (3.5–6), 6 (5–8), 9 (6–11), and 11 (9–14) per day in those receiving 3, 4, 5, and 6 antihypertensive drug classes, respectively. Diuretics were used in 425 patients, but not counted as one antihypertensive drug class.

3.3 | Apparent treatment-resistant hypertension based on higher office blood pressure threshold

According to ACC/AHA guideline, home BP is suggested to define aTRH, however, many studies have used office BP.[7,13,14] We also collected office BP and used 140/90 mmHg threshold to evaluate aTRH. As shown in Table 2, the prevalence was 37.3% based on this criterion, which was lower than that on home BP (42.2%).

3.4 | Drug adherence and resistant hypertension in peritoneal dialysis patients

We also surveyed drug adherence to evaluate the relative RH in one PD center. Among 283 PD hypertensive patients who completed the MMAS-8 questionnaire, the proportion of medium/high drug adherence to anti-hypertensive therapy was 89.8% (254 patients, MMAS-8 scores ≥6). And of the 115 patients who completed pill counting, 86 patients (74.8%, pill counting rate ≥80%) were classified as high drug adherence. The prevalence of RH was 40.6% and 41.9% among those with medium/high adherence based on the MMAS-8 scores and the pill counting rate, separately (Table S3).

3.5 | Related factors of apparent treatment-resistant hypertension

We finally analyzed the related factors of aTRH. As expected, younger males, smokers and drinkers, lower weekly Kt/V score, and higher BMI were related to higher aTRH incident. Serum creatinine, albumin, and blood hemoglobin were also associated with aTRH. After adjusted with demographic characteristics (age, sex, BMI, diabetes, smoker, and drinker), dialysis indicators (dialysis vintage, RRF, ultrafiltrated volume, dialysate glucose, and Kt/V), biochemical examinations (serum creatinine and blood hemoglobin), and ESA dosage, dialysis adequacy and serum albumin were still negatively related to aTRH (Table 3).

4 | DISCUSSION

In this multi-center cross-sectional study based on home BP monitoring, we have confirmed the pervasive nature of hypertension and the high prevalence of aTRH in PD patients. About two in five occurred aTRH in PD hypertensive patients. The aTRH prevalence based on home and office BP was similar to each other. Dialysis adequacy and

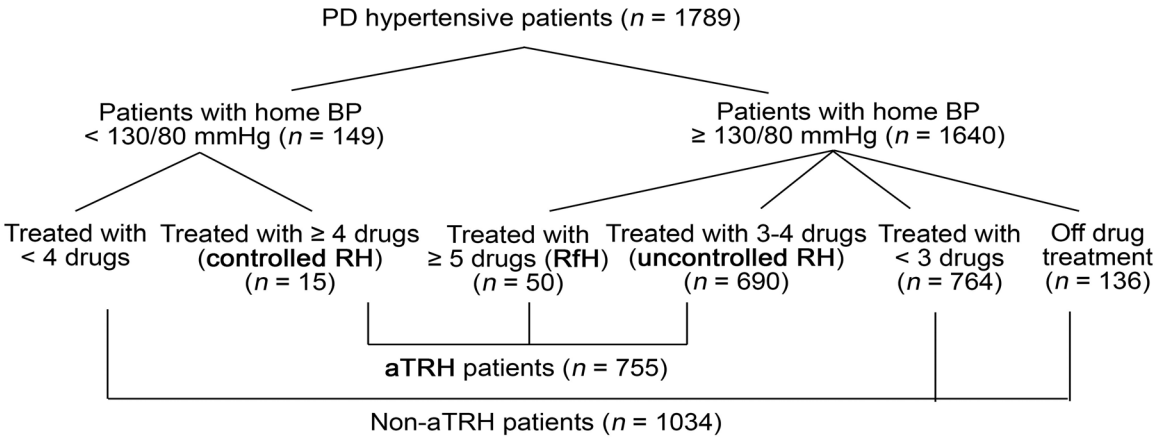

FIGURE 2 PD hypertensive patients divided in aTRH (including uncontrolled RH, controlled RH and RfH) and non-aTRH groups according to home BP levels and number of anti-hypertensive drugs used. PD, peritoneal dialysis; BP, blood pressure; RH, resistant hypertension; RfH, refractory hypertension; aTRH, apparent treatment-resistant hypertension

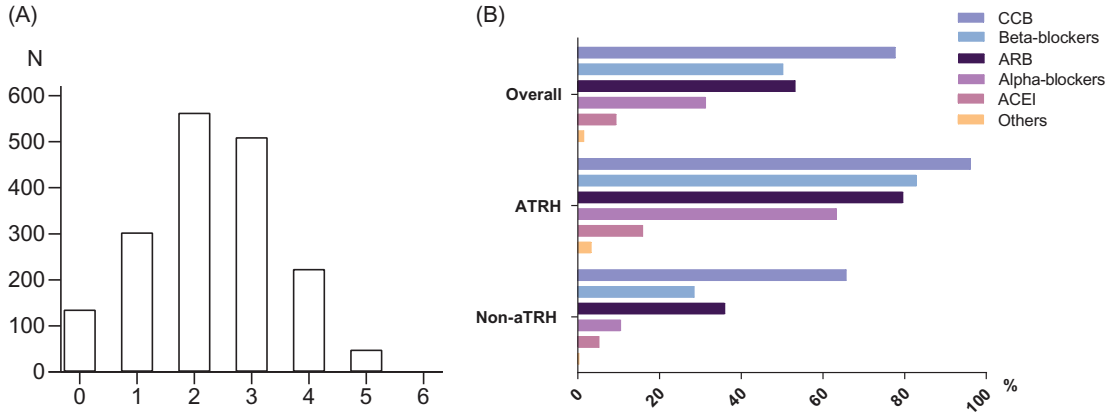

FIGURE 3 Distribution of antihypertensive drug classes (A) and frequency of antihypertensive medication use (B) in PD patients. Classes of anti-hypertensive drug ranged from 0 to 6 (median: 2, IQR: 1–3) in the part A. Frequency of anti-hypertensive medication use among overall patients, patients with aTRH and non-aTRH were presented in part B. PD, peritoneal dialysis; aTRH, apparent treatment-resistant hypertension; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; IQR, interquartile range

serum albumin seemed to be tightly associated with aTRH. These data presented a serious problem about hypertension management in PD patients.

ATRH is considered as a common problem in hypertensive population with a prevalence ranging from 0.5% to 14.3%.[11] In predialysis CKD patients (stage 3–5), this prevalence significantly increases to 1.6%–24.7%,[11] and up to 42% in some population-based studies.[29] Furthermore, with the restricted application of anti-hypertensive drugs and the limited effect of diuretics, the proportion is rising with the progression of CKD.[13,30] When CKD patients receive renal replacement treatment, fluid overload would be a growing problem because of residual renal function loss and dietary relaxation, which is a central feature of RH.[11 31] While few patients have the evidence of predialysis fluid overload because of the effective water and metabolic waste clearance by regular hemodialysis.[14,32,33] Thus, HD patients have a similar aTRH prevalence of 18%–24% to the predialysis CKD patients.[1,11,14] Our data in HD patients reconfirmed the aTRH prevalence of 16.9% (data were not shown). In patients undergoing PD, the sodium and water retention becomes a prominent problem due to inefficient peritoneal transportation, especially in those with peritonitis and micro-inflammation, long term glucose exposure, and peritoneal fibrosis.[16,34,35] Hence, the aTRH incident might be higher in this population. However, data focused on PD population are lacking. After surveyed from nine units in Guangdong Province, we found that about 1789 (95.6%) PD patients have hypertension, and the aTRH prevalence was 42.2%. This proportion is very high and surprising, but is in expected.

Even though the recommended target SBP level for adults with CKD is 120 mmHg,[36] the threshold of 130/80 mmHg is still the most commonly used one to define aTRH, and the BP should be based on out-of-office measurements (e.g., home BP).[20] However, threshold of ESRD patients undergoing dialysis has not mentioned in these

TABLE 1 Clinical characteristics of PD hypertensive patients with or without aTRH

Characteristics	Overall	Non-aTRH	aTHR	*P*-Value[a]
N	1789	1034	755	–
Male (*n* [%])	949 (53.0)	505 (48.8)	444 (58.8)	<0.001
Age (years)	49.8 ± 13.5	50.8 ± 13.8	48.4 ± 13.0	<0.001
BMI (kg/m^2)	22.7 ± 3.6	22.5 ± 3.7	23.0 ± 3.4	0.002
Diabetes (*n* [%])	346 (19.3)	204 (19.7)	142 (18.8)	0.626
Smoker (*n* [%])	286 (17.0)	144 (14.8)	142 (19.9)	0.005
Drinker (*n* [%])	153 (9.1)	77 (7.9)	76 (10.7)	0.051
With RRF (*n* [%])	1124 (64.0)	675 (66.4)	449 (60.8)	0.014
Home SBP (mmHg)	141.1 ± 16.0	136.7 ± 14.9	147.3 ± 15.2	<0.001
Home DBP (mmHg)	86.7 ± 10.9	84.8 ± 10.4	89.1 ± 11.1	<0.001
Office SBP (mmHg)	143.4 ± 18.2	139.0 ± 17.3	149.3 ± 17.6	<0.001
Office DBP (mmHg)	87.2 ± 12.6	85.7 ± 11.8	89.4 ± 13.3	<0.001
Lab examinations				
Serum creatinine (mg/dl)	11.2 ± 3.4	10.8 ± 3.4	11.8 ± 3.3	<0.001
Serum albumin (g/dl)	3.6 ± 0.5	3.7 ± 0.5	3.6 ± 0.5	<0.001
Blood hemoglobin (g/dl)	10.5 ± 2.1	10.6 ± 2.0	10.3 ± 2.1	0.001
Baseline PD characteristics				
CAPD (*n* [%])	1725 (96.4)	997 (96.4)	728 (96.4)	0.998
PD vintage (months)	26 (11-50)	24 (10-50)	27 (12-48)	0.760
UF volume (L/d)	0.5 (0.2-0.8)	0.5 (0.2-0.8)	0.6 (0.3-0.9)	<0.001
Urine volume (L/d)	0.3 (0-0.7)	0.3 (0-0.8)	0.3 (0-0.6)	0.001
Dialysate GLUC (%)	1.81 ± 0.34	1.79 ± 0.34	1.84 ± 0.34	0.003
Kt/V score	1.95 ± 0.57	2.01 ± 0.57	1.86 ± 0.55	<0.001
PET type[*]				0.007
High (*n* [%])	143 (10.1)	69 (8.5)	74 (12.4)	–
High average (*n* [%])	660 (46.7)	366 (45.0)	294 (49.2)	–
Low average (*n* [%])	538 (38.1)	337 (41.4)	201 (33.6)	–
Low (*n* [%])	71 (5.0)	42 (5.2)	29 (4.8)	–
ESA dosage (1000U/week)	7 (2.5-10)	6 (2-10)	7.8 (5-10)	<0.001

Note: Data of overall patients, patients with aTRH and non-aTRH were presented as numbers and percentages, means and standard deviations, or median and interquartile range. KT/V, and PET were calculated by formulas mentioned before. PD, peritoneal dialysis; aTRH, apparent treatment-resistant hypertension; BMI, body mass index; RRF, Residual renal function; SBP, systolic blood pressure; DBP, diastolic blood pressure; CAPD, continuous ambulatory peritoneal dialysis; UF, ultrafiltration; GLUC, glucose concentration; PET, peritoneal equilibration test, ESA, erythropoiesis-stimulating agents.

[a]PET type based on 1428 PD hypertensive patients including 863 nonaTRH patients and 565 aTRH patients.

*P for comparisons between aTRH and nonaTRH patients by t-test, Kruskal–Wallis test, or Chi-squared tests for continuous and categorical variables, respectively.

guidelines due to the lack of data. In our study, we used the threshold of 130/80 mmHg based on home BP to evaluate aTRH in PD hypertensive population, and obtained a very high prevalence of 42.2%. Recently, one study from HD population has used the threshold of 140/90 mmHg based on office BP to define the aTRH.[14] Therefore, we also collected the office BP and tried this threshold. Unexpectedly, the prevalence of aTRH was 37.3% when using office BP threshold of 140/90 mmHg, which was lower than that using home BP criterion. In the era of mercury sphygmomanometer, patients needed to stay in the office and directly face doctors or nurses directly, so there would be a higher measured blood pressure level, which was a major reason for white coat hypertension.[37] Recently, electronic sphygmomanometers have been widely used all over the world, including China.[38] In this way, blood pressure can be measured automatically in a separate space without doctors or nurses, which might greatly reduce the effect of white coat hypertension.[39] Additionally, BP is measured according to the standard KDIGO guidelines.[36] All of these narrows the difference between office and home BP. In our population, home and office BP was similar to each other (Table 1), which indicated that office BP might be infinitely close to home BP by standard measurement program and electronic sphygmomanometer in a separate space. This might be the reason why aTRH prevalence significantly decreased when using

TABLE 2 ATRH prevalence based on higher office BP threshold

BP thresholds	aTRH, *n* (%)
Home BP 130/80 mmHg[a]	755 (42.2)
Office BP 140/90 mmHg[b]	667 (37.3)

Abbreviations: aTRH, apparent treatment-resistant hypertension; BP, blood pressure; ACC/AHA, American College of Cardiology/American Heart Association; EURECA-m, European Renal and Cardiovascular Medicine.
[a]Definition of aTRH using 2017 ACC/AHA threshold (home BP ≥ 130/80 mmHg).
[b]Definition of aTRH using EURECA-m thresholds (office BP ≥ 140/90 mmHg).

higher office BP threshold (140/90 mmHg). Regardless, we suggested to define aTRH using the lower home BP threshold of 130/80 mmHg in PD population for more attention to hypertension management.

Sodium and water retention is a major causation of aTRH,[31] especially in patients with CKD.[11] This might be the reason why diuretics are considered as a necessary criterion to define aTRH.[40] However, with the residual renal function loss and anuria, diuretics might not work in patients undergoing dialysis.[18,19] In the study from HD patients, diuretics was not considered as one anti-hypertensive class.[1] In our study, 36.1% PD patients were anuria, the average 24-h urine volume was 0.3 (0–0.7) liters, and only 22.7% PD patients have received diuretics. When considered diuretics as one anti-hypertensive class, the prevalence of aTRH was 50.4% (data were not shown). Due to the inefficiency of diuretics in PD patients,[18,19] it might be an illusion of high aTRH prevalence when counting diuretics as one class. Therefore, we have not counted diuretics as anti-hypertensive drugs.

Drug adherence is another major factor of pseudo-resistance.[5] Consistent adherence to anti-hypertensive medications is the cornerstone for achieving hypertension control. Optimal drug adherence could decrease the risk of adverse cardiovascular events, and reduce unnecessary prescribing and economic burden on the health care system in hypertensive population.[41] MMAS-8 is generally regarded as a subjective self-reported medication adherence, while pill counting is a kind of objective method for assessing medication adherence.[28] However, it might not be easy to acquire high quality response from multi-center study, either from subjective patients' questionnaire or from objective pill counting directly. We have tried to collect the drug adherence from all centers, but the quality was not very good. Thus, we have reported the drug adherence of our center. Because of the very small sample-size, the result could not represent true RH. Lager sample-size studies should be conducted to survey it.

In general hypertensive population studies, it was found that men, older, alcohol intake, and higher BMI were associated with aTRH.[42,43] In some studies, younger patients were related to higher aTRH prevalence.[14] To date, association of aTRH has not mentioned in ESRD patients undergoing dialysis.[1,14] In our population, younger and higher BMI were associated with higher aTRH incident. In addition, nutritional status and dialysis adequacy were closely related to aTRH. Better nutritional status and adequate dialysis are needed in hypertension management in PD patients.

This study had several limitations. The first limitation is the representativeness of the population. Patients were mainly recruited from

TABLE 3 Related factors of aTRH in PD hypertensive patients

	Unadjusted		Adjusted[a]	
	OR (95% CI)	*P*-Value	OR (95% CI)	*P*-Value
Age (per 1-year increment)	0.99 (.98-.99)	<0.001	0.98 (0.97-0.99)	0.001
Male (vs. female)	1.50 (1.24-1.81)	<0.001	1.26 (0.95-1.68)	0.108
BMI (per 1-kg/m^2 increment)	1.04 (1.02-1.07)	0.002	1.04 (1.01-1.08)	0.022
PD vintage (per 1-month increment)	0.99 (0.99-1.00)	0.412	1.05 (0.93-1.19)	0.440
Diabetes (vs. no)	0.94 (0.74-1.20)	0.626	0.79 (0.57-1.08)	0.133
Smoker (vs. no)	1.44 (1.11-1.85)	0.005	1.14 (0.79-1.66)	0.489
Drinker (vs. no)	1.39 (1.00-1.94)	0.051	1.07 (0.68-1.70)	0.764
With RRF (vs. no)	0.78 (0.64-0.95)	0.014	1.03 (0.78-1.36)	0.828
Serum creatinine (per 1-mg/dl increment)	1.10 (1.07-1.13)	<0.001	1.04 (0.99-1.08)	0.121
Serum albumin (per 1-g/dl increment)	0.65 (0.53-0.80)	<0.001	0.51 (0.39-0.68)	<0.001
Blood hemoglobin (per 1-g/dl increment)	0.93 (0.89-.0 97)	0.001	1.01 (0.95-1.07)	0.791
UF volume (per 1-L/d increment)	1.19 (1.03-1.36)	0.015	1.05 (0.89-1.24)	0.563
Dialysate GLUC (per 1% increment)	1.54 (1.15-2.06)	0.004	1.13 (0.78-1.63)	0.525
Kt/V (per 1 increment)	0.59 (0.49-0.72)	<0.001	0.75 (0.57-0.98)	0.035
ESA dosage (per 1000 U/week increment)	1.02 (0.99-1.05)	0.175	1.01 (0.97-1.04)	0.654

Abbreviations: aTRH, apparent treatment-resistant hypertension; PD, peritoneal dialysis; BMI, body mass index; RRF, residual renal function; UF, ultrafiltration; GLUC, glucose concentration; ESA, erythropoiesis-stimulating agents.
[a]Adjusted for age; sex; BMI; dialysis vintage; diabetes; smoker; drinker; RRF; serum creatinine; serum albumin; blood hemoglobin; UF volume; dialysate GLUC; Kt/V; and ESA dosage.

Guangdong PD units. Therefore, this study could only represent the PD aTRH prevalence of Guangdong province, or parts of South China, but not that of the whole China. Further studies including the whole China and even larger PD population should be conducted for the exact aTRH evaluation. The second limitation is about the anti-hypertensive drug adherence assessment. Only 15% patients have been involved in the MMAS-8 and pill counting studies. Lager sample-size and even higher quality studies about drug adherence should be conducted. Third, the ambulatory BP monitoring data has not been collected to define aTRH in this study. Even though ambulatory BP monitoring might not be universally tolerated in dialysis patients which might cause selection bias, it remains the preferred method recommended in the guides.[20] However, home BP monitoring is also suggested.[20] Fourth, the data of salt intake in PD patients has not been evaluated. The three-day dietary record and 24-h urinary sodium excretion are the most common methods to evaluate salt intake. However, 24-h urinary sodium excretion might not be suitable for salt intake evaluation for PD because most patients are oliguria or anuria.[18,19] The three-day dietary record, a perfect tool to evaluate salt intake, is relatively difficult for us in our multicenter cross-sectional study. In our PD population, all patients have been educated to take low-salt diet. The data from our center based on three-day dietary record have shown the low-salt level of PD patients (2.1 ± 1.4 g/d of sodium, and 5.3 ± 3.4 g/d of salt),[44] which might partially represent the degree of salt intake in PD population. Finally, we are not able to assess the effect of hypertension resistance to long term prognosis in PD population according to this cross-sectional study. Retrospective and prospective cohort studies are needed.

5 | CONCLUSIONS

In conclusion, our present study demonstrated that aTRH was very common in PD hypertensive patients with the prevalence of 42.2%, which is much higher than that in HD population. Dialysis adequacy and nutritional status were tightly associated with aTRH. More attention should be paid to hypertension management in PD population.

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CONFLICT OF INTEREST DISCLOSURE

The authors report no conflicts of interest.

AUTHOR CONTRIBUTIONS

Jun Ai, Zhihao Huo, Danyang Liu and Dan Li conceived and designed the analysis. Dan Li performed the analysis. Jun Ai, Danyang Liu and Dan Li wrote the manuscript draft. Jun Ai, Fuhua Lu, and Guangqing Zhang revised for critical intellectual content. All authors contributed to data collection, reviewed, and edited the manuscript for important intellectual content. All authors approved of the final manuscript for submission.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Not available.

CLINICAL TRIAL REGISTRATION

Not available.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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