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Effectiveness and Safety of Macitentan in Hemodialysis Patients with Pulmonary Hypertension: A Retrospective and Observational Study

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Abstract: *Background:* Pulmonary hypertension (PH) is a rare disease often associated with high mortality and is recently recognized as a common complication secondary to chronic kidney disease. Macitentan can improve clinical outcomes in patients with pulmonary artery hypertension in clinical trials. To observe the clinical efficacy and safety of macitentan tablets in the treatment of hemodialysis HD patients complicated with PH. *Methods:* This was a retrospective study performed in the renal division of Shaanxi Provincial People's Hospital between January 1, 2024, and December 31, 2025. A total of 10 patients with PAH who underwent regular hemodialysis (HD) (three times weekly for 4 hours each session) were enrolled. All patients received basic treatment, based on which macitentan tablets were added (10 mg per dose, once daily, oral administration), with a treatment cycle of 12 weeks. The 6-minute walk distance (6MWD), pulmonary artery systolic pressure (PASP) measured by echocardiography, and WHO functional class were compared before and after treatment. Serious adverse events (SAEs) and adverse drug reactions (ADRs) of macitentan were collected. *Results:* After 12 weeks of treatment, the proportion of patients with WHO-FC II increased from 20% to 60% ($p = 0.046$). LVEF showed an upward trend, with the median rising from 50.5% to 53.5% ($p = 0.03$). The mean 6MWD increased by 28.8 m ($p = 0.035$). Median NT-proBNP decreased from 39018 ng/L to 18987.5 ng/L ($p = 0.017$). Meanwhile, mean PASP dropped from 52.1 (5.363) mmHg to 39.4 (8.796) mmHg. Only two mild adverse reactions (dizziness and aggravated mild anemia) occurred during the entire observation period, which were relieved after symptomatic treatment. No severe liver or renal function impairment or treatment discontinuation was observed. *Conclusion:* With regular HD and basic treatment, macitentan demonstrates clear short-term efficacy and controllable safety in HD patients with WHO class II-III PH.

Keywords: Macitentan; Hemodialysis (HD); Pulmonary hypertension (PH)

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1. Introduction

Pulmonary arterial hypertension (PAH) is a chronic and progressive disease characterized by the presence of precapillary pulmonary hypertension [1,2]. The disease results from functional and structural changes in the pulmonary vasculature, leading to increased pulmonary vascular resistance, right ventricular failure, and subsequently death [3,4]. In the general population, the prevalence of PAH is estimated to be 15-50 cases per million, with an annual incidence rate of approximately 2.4 cases per million [5]. However, pulmonary hypertension (PH) affects 21% to 41% of patients with chronic kidney disease (CKD) and up to 60% of patients with kidney failure receiving hemodialysis [6,7]. Mechanisms responsible for PAH in HD patients have not been completely understood. However, abnormal endothelium-dependent vasodilatation, vascular calcification, thromboembolic disease, hypervolemia, increased pulmonary vascular flow due to the presence of arterio-venous fistulas, anemia and sleep-disordered breathing play a role [8,9]. The classic symptoms of PAH occur relatively late and may be confounded by overhydration in HD patients, leading to the delayed diagnosis and the worsening of prognosis [10]. To date, there are no targeted treatments for PH in patients with CKD. Macitentan, as an endothelin receptor antagonist, was approved by the China National Medical Products Administration in 2018 as a monotherapy or combination therapy for the treatment of adult patients with PAH. The approval was mostly based on findings from the global SERAPHIN trial, and the drug is currently indicated for patients with PAH and preserved renal function. However, limited data are available regarding the application of macitentan in patients undergoing hemodialysis. The present study aims to evaluate the effectiveness and safety of macitentan prescribed to patients undergoing hemodialysis complicated with PAH.

2. Methods

2.1. Study design and participants

The retrospective study was performed in the renal division of Shaanxi Provincial People's Hospital between January 1, 2024, and December 31, 2025. A total of 10 patients with PAH who underwent regular hemodialysis (HD) (three times weekly for 4 hours each session) were enrolled. All patients were treated with high-flux dialyzers, with a blood flow of 250–300 mL/min and a dialysate flow of 500 mL/min.

Patients were eligible if they had confirmed by echocardiography (pulmonary artery systolic pressure, PASP ≥ 35 mmHg) and conforming to WHO functional class II-III, were aged 18 years old, had received regular hemodialysis (HD) for ≥ 3 months, and had available data in their medical chart for data collection, with follow-up data available at 3–6 months. All enrolled patients were given basic treatments, including correction of anemia with erythropoietin, iron supplementation, and improvement of heart failure with ACEI/ARB drugs.

Patients with the following conditions were excluded: allergy to macitentan or drug excipients; pregnant, lactating women or those with pregnancy plans; severe liver function impairment (Child-Pugh class C); acute myocardial infarction, cerebral hemorrhage or severe infection occurring within the past 1 month; expected survival time < 6 months.

All patients maintained their original HD regimen and basic treatment. On this basis, Macitentan Tablets were additionally administered (dosage: 10 mg per time, once a day, taken orally). On dialysis days, the medication time should avoid the dialysis process, which is fixed at 2 hours before dialysis or 4 hours after dialysis to prevent drug clearance from affecting the blood drug concentration. The continuous treatment

duration was 12 weeks.

Written informed consent was obtained from all patients. The trial adhered to the Declaration of Helsinki and the research protocol was approved by local institutional review boards or independent ethics committees.

2.2. Clinical and laboratory data collection

Patient data on baseline characteristics (age, gender, medication used), etiology of CKD, laboratory tests and hemodynamics were recorded.

Before treatment, 4 weeks, 8 weeks, and 12 weeks after treatment, the following items were monitored respectively: (1) Renal function: serum creatinine and blood urea nitrogen, with pre-dialysis and post-dialysis values recorded; (2) Routine blood test: hemoglobin and hematocrit; (3) Liver function: alanine aminotransferase (ALT) and aspartate aminotransferase (AST); (4) Electrolytes: serum potassium and serum sodium; (5) Adverse reactions (such as dizziness, headache, rash, edema, etc.) and corresponding treatment measures were recorded in detail.

Before treatment and 12 weeks after treatment, the following indicators were measured respectively: (1) 6-minute walk distance (6MWD): conducted in a 20-meter flat corridor in accordance with standard procedures, and the maximum walking distance was recorded; (2) Echocardiography: a GE Vivid E95 color Doppler ultrasound machine was used to estimate the pulmonary artery systolic pressure (PASP) through the tricuspid regurgitation velocity; (3) WHO functional classification: evaluated based on the patient's dyspnea and fatigue degree after daily activities.

2.3. Data analysis

All statistical analyses were performed using the SPSS 27.0 software. Continuous data were summarized as median and mean (SD), and categorical data were summarized as data counts (percentage). For the comparison of count data before and after treatment, if the difference is close to a normal distribution, the paired *t*-test was used; if the normal distribution is not satisfied, the Wilcoxon signed-rank test was adopted. The P-value < 0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

A total of 10 patients were screened, and 2 patients who met the eligibility criteria were identified. Two patients were excluded: one discontinued macitentan voluntarily after 1 month, and the other lacked complete follow-up data. Patient demographics and disease characteristics are shown in **Table 1**.

Table 1. Summary of patient characteristics

Characteristics	All patients
	Total (N=10)
Female, n(%)	2 (20%)
Age, mean (SD)	49.3 (10.57)
Time of dialysis(months)	12 (10,19)
Underlying disease	

Characteristics	All patients
Glomerulonephritis	4 (40%)
Diabetic nephropathy	2 (20%)
Hypertensive nephropathy	2 (20%)
purpura nephritis	1 (10%)
Unknown	1 (10%)
Time since diagnosis, mean(SD), months	7 (4,10)
Prior PHA target therapy, n(%)	
Targeted-therapy native	9 (90%)
Targeted-therapy	1 (10%)

Patient demographics and disease characteristics are shown in **Table 1**. The mean (SD) age of the patients at baseline was 49.3 (10.57) years old, with 20% being females and the duration of dialysis and PAH diagnosis presented a skewed distribution, which was expressed as median (interquartile range), with the median dialysis duration of 12 months and the median time since PAH diagnosis of 7 months. Regarding the underlying diseases, 4 cases (40.0%) were glomerulonephritis, 2 cases (20.0%) were diabetic nephropathy, 1 case (10.0%) was purpura nephritis, and 1 case (10.0%) had an unknown underlying disease. In terms of treatment history, 9 patients (90.0%) were naive to targeted therapy for PAH, and only 1 patient (10.0%) had received prior targeted therapy. All patients received regular hemodialysis. The changes in clinical and laboratory parameters between baseline and post-treatment were compared in **Table 2**.

Table 2. Comparisons of patient characteristics before and after macitentan treatment

Measures	Baseline	First follow-up	*p* value
HB (g/L)	108.5 ± 26.142	110.1 ± 12.957	0.799
ALB (g/L)	35.470 ± 4.469	37.890 ± 3.174	0.086
ALT (U/L)	10.300 ± 3.129	13.100 ± 5.021	0.079
AST (U/L)	9.600 ± 2.757	12.6 ± 4.742	0.122
SCr (umol/L)	710.36 ± 160.634	776.810 ± 244.547	0.334
BUN (mmol/L)	15.36 (13.250, 22.323)	20.170 (14.098, 22.438)	0.799
K (mmol/L)	4.770 ± 0.868	4.660 ± 0.759	0.613
Na (mmol/L)	140.300 ± 3.466	139.500 ± 4.378	0.574
NT-proBNP (ng/L)	39018 (27674.5, 84285.5)	18987.5 (12801.5, 37959.75)	0.017
PASP	52.100 ± 5.363	39.400 ± 8.796	0.002
LVEF%	50.500 (35.00, 59.25)	53.500 (45.25, 60.75)	0.03
RVEDD (mm)	27.100 ± 2.079	26.200 ± 1.814	0.108
LVEDD (mm)	60.400 ± 11.796	59.500 ± 10.835	0.147
WHO-FC, n(%)	3 (2.75, 3)	2 (2, 3)	0.046
6MWD (mm)	234.600 ± 66.562	263.400 ± 78.062	0.035

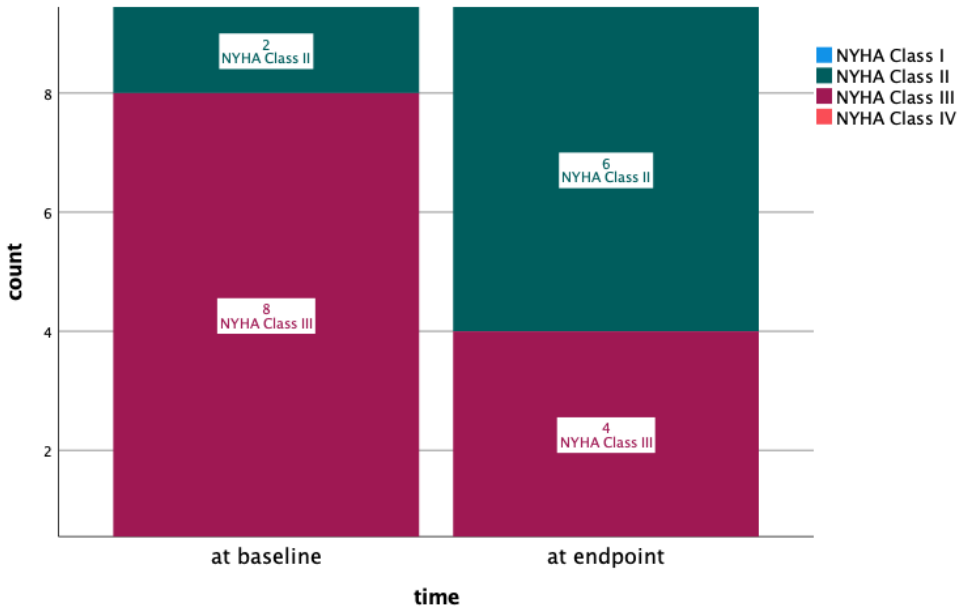

Figure 1. Change from baseline in WHO-FC at the 3-month follow-up visit.

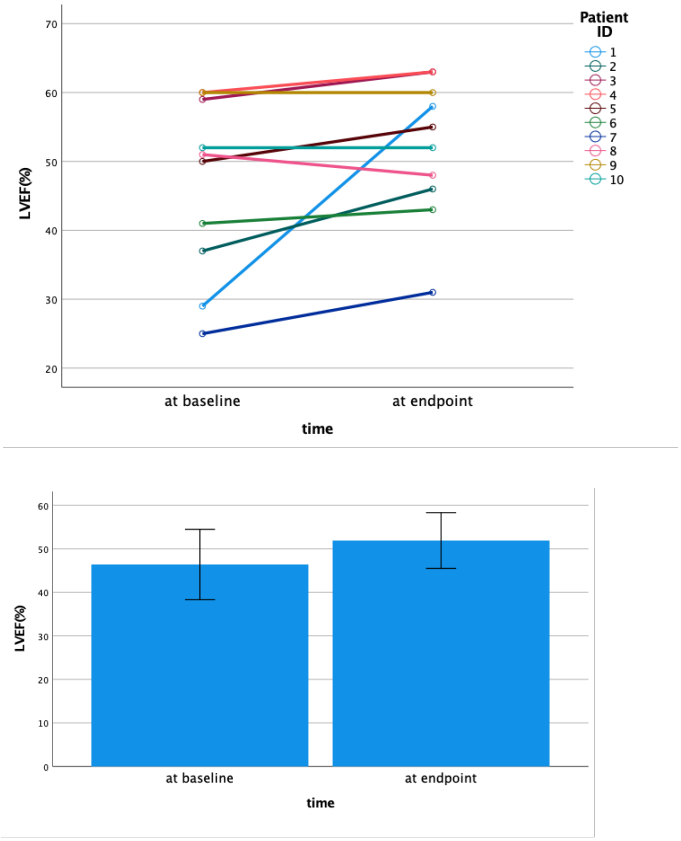

Figure 2. Change from baseline in LVEF at the 3-month follow-up visit.

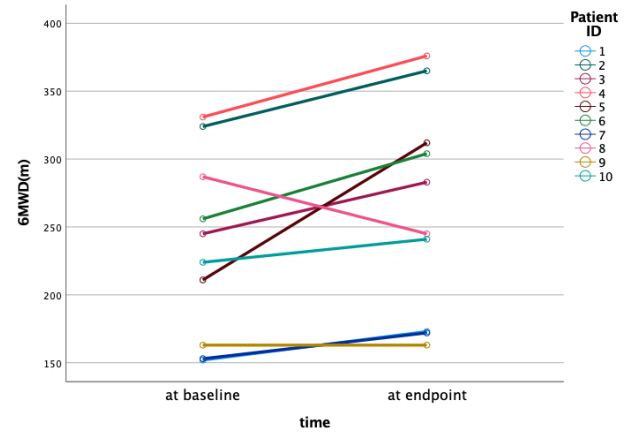

Figure 3. Change from baseline in 6MWD at the 3-month follow-up visit.

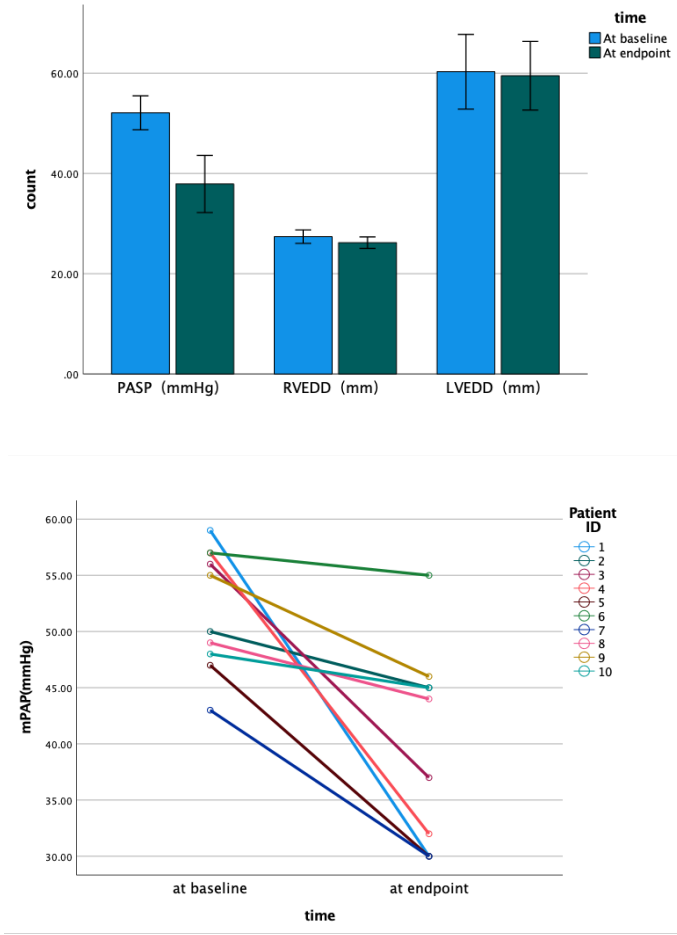

Figure 4. Change from baseline in mPAP at the 3-month follow-up visit.

3.2. Improvements in WHO-FC, 6MWD, LVEF and NT-proBNP

A total of 4 patients demonstrated improved [(n = 4), 40%] or maintained [(n = 2), 20%] WHO-FC compared to baseline (**Figure 1**). The proportion of patients with WHO-FC II changed from 20% to 60% from baseline

at the 3-month follow-up visit (p = 0.046). An increasing trend in the LVEF levels was also observed (**Figure 2**), with the median changing from 50.5% to 53.5% (p = 0.03). The mean (SD) change in 6MWD from baseline to month 3 follow-up was 28.8m (p = 0.035). An increase in 6MWD was observed in 7 (70%) patients, and 1 (60%) had 6MWD maintained (**Figure 3**). One patient developed a mild upper respiratory tract infection at week 8 of treatment, with a transient decrease in 6MWD from 287 m at baseline to 245 m. The 6MWD recovered to 274 m after full resolution of the infection. Significant decreases were observed in NT-proBNP levels from baseline, with median changing from 39018 ng/L to 18987.5 ng/L (p = 0.017).

3.3. Improvements in PASP

Mean (SD) PASP decreased from 52.1 (5.363) mmHg to 39.4 (8.796) mmHg from baseline at the 3-month follow-up visit. A decrease in PASP exceeding 10 mmHg was noted in half of the enrolled patients, with four patients achieving complete normalization of pulmonary artery pressure (**Figure 4**).

3.4. Safety

None of the 10 patients experienced death or serious adverse events during the entire treatment course. All patients-maintained ALT and AST levels within the normal range throughout the treatment period. Serum creatinine and blood urea nitrogen levels before and after dialysis showed no significant differences compared with baseline (p > 0.05). One patient experienced a decrease in hemoglobin from 96 g/L to 85 g/L at week 6 of treatment. Further evaluation confirmed mild blood loss caused by minor dialyzer leakage. After increasing the dose of erythropoietin from 6000 U/week to 10 000 U/week, the hemoglobin level recovered to 98 g/L at week 12 of treatment. A total of two mild adverse events occurred, accounting for an incidence of 20%. One patient developed orthostatic dizziness at week 4 of treatment, with supine blood pressure of 130/80 mmHg and upright blood pressure of 110/70 mmHg, and no syncope. After the dosage of the calcium channel blocker amlodipine was reduced from 5 mg daily to 2.5 mg daily, the dizziness completely resolved. The other patient presented with aggravated mild anemia as described above. No severe adverse reactions such as rash, edema, or hepatic injury were observed. All patients completed the 12-week treatment, and no participant discontinued the study medication.

4. Discussion

This retrospective review study showed that improvements in WHO-FC, 6MWD and and pulmonary arterial hypertension for hemodialysis patients with pulmonary arterial hypertension (PAH) and New York Heart Association (NYHA) functional class II-III treated with macitentan. The therapeutic effect was consistent with the efficacy trend of previous endothelin receptor antagonists (ERA) in non-dialysis patients with pulmonary arterial hypertension [11–13]. Since there are few previous reports on the use of macitentan in dialysis patients, the findings of this study will serve as a valuable reference for the clinical management of hemodialysis patients with PAH.

The improvements in WHO-FC, 6MWD, and NT-proBNP with macitentan at 3 months in the present study add to the growing body of evidence that supports the efficacy of macitentan in dialysis patients. In our study, we also observed numerical improvements in PASP measured by echocardiography from baseline to 3-month follow-ups. These findings build on previous evidence that macitentan improves right ventricular function and hemodynamic parameters [14,15].

From the mechanistic perspective, pulmonary hypertension in hemodialysis patients is mainly driven by uremic toxins (indoxyl sulfate, p-cresol) that stimulate vascular endothelial cells and markedly upregulate ET-1 secretion. ET-1 triggers severe pulmonary vasoconstriction via ET-A receptors and promotes pulmonary vascular smooth muscle proliferation and collagen deposition through ET-B receptors, further accelerating pulmonary vascular remodeling [16,17]. As a dual endothelin receptor antagonist, macitentan blocks both ET-A and ET-B, acutely alleviating pulmonary vasoconstriction and lowering PASP, while chronically inhibiting vascular remodeling to maintain long-term efficacy [18,19]. In the present study, 50% of patients achieved a notable PASP reduction, and 60% improved from WHO functional class III to class II, supporting the mechanistic benefits of macitentan in hemodialysis populations. Moreover, reduced PASP decreases right ventricular afterload, optimizes right cardiac output, and improves exercise tolerance, with a mean 6MWD increase of 28.8 m. Consistent with improved cardiac functional classification, these findings indicate that macitentan can effectively ameliorate right ventricular dysfunction in hemodialysis patients.

The Adverse Drug Reactions and Serious Adverse Events observed in our study were consistent with the well-known side effects associated with approved ERAs. Regarding safety, the prescribing information for macitentan indicates that the drug is predominantly excreted via the biliary route, with only about 10% undergoing renal elimination. As hemodialysis patients, particular attention was paid to the potential risk of drug accumulation in this population. No renal function deterioration or liver injury related to drug accumulation was identified in the present study. As demonstrated in previous studies, macitentan has a favorable renal and liver safety profile [19,20]. In the study, only one patient experienced dizziness, which was considered associated with concurrent antihypertensive therapy, and one patient exhibited aggravated anemia, likely attributable to dialyzer leakage. Both symptoms were alleviated following symptomatic intervention, suggesting favorable short-term tolerability of macitentan among hemodialysis patients. Regular monitoring of liver function, blood pressure, and routine blood parameters during treatment can minimize the incidence of adverse reactions.

Our study has several limitations. Firstly, the small sample size, single-center setting and absence of a control group may lead to selection bias in our findings. Secondly, the observation period was only 12 weeks. Long-term efficacy and safety require further investigation with expanded samples and prolonged follow-up. Thirdly, macitentan plasma concentrations were not determined, thus limiting definitive assessment of the specific impact of hemodialysis on drug exposure.

In conclusion, macitentan is an effective therapeutic option for HD patients with WHO functional class II-III pulmonary hypertension. It improves exercise tolerance and cardiac function in the short term with a favorable safety profile. For clinical application, joint assessment by nephrology and respiratory/cardiology departments is recommended to strictly exclude contraindications, including pregnancy and hypersensitivity. Concomitant administration with CYP3A4 inhibitors such as ketoconazole should be avoided to prevent elevated drug concentrations. Long-term monitoring of blood routine, liver and renal function, and PASP is warranted, with dosing time adjusted in accordance with dialysis schedules to optimize efficacy and safety.

5. Conclusion

This study provides a rationale for the targeted use of macitentan in clinically stable hemodialysis patients with WHO functional class II–III pulmonary hypertension. Following 12 weeks of add-on macitentan 10 mg once daily alongside maintenance hemodialysis and optimized standard care, significant improvements

were observed in 6MWD, pulmonary artery systolic pressure, and WHO functional class, with favorable short-term safety and tolerability irrespective of the underlying nephropathy. Dosing schedules should be individualized to avoid concurrent dialysis to preserve therapeutic drug levels. Long-term prospective evaluation with serial assessment of calcium-phosphorus metabolism and bone mineral density is encouraged to fully characterize the long-term efficacy and safety of macitentan in this high-risk population.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Humbert M, Gibbs S, Lang I, et al., 2023, The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology and the European Respiratory Society Endorsed by Association for European Paediatric and Congenital Cardiology and International Society for Heart and Lung Transplantation. European Heart Journal, 43(38): 3618–3618.

[2] Badesch DB, Champion HC, Gomez Sanchez MA, et al., 2009, Diagnosis and Assessment of Pulmonary Arterial Hypertension. Journal of the American College of Cardiology, 54(1): S55–S66.

[3] Humbert M, Morrell NW, Archer SL, et al., 2004, Cellular and Molecular Pathobiology of Pulmonary Arterial Hypertension. Journal of the American College of Cardiology, 43(12): S13–S24.

[4] Seferian A, Simonneau G, 2013, Therapies for Pulmonary Arterial Hypertension Where Are We Today Where Do We Go Tomorrow. European Respiratory Review, 22(129): 217–226.

[5] Humbert M, Kovacs G, Hoeper MM, et al., 2023, 2022 ESC ERS Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension. European Respiratory Journal, 61(1): 2200879–2200879.

[6] Zhang Q, Wang L, Zeng H, et al., 2018, Epidemiology and Risk Factors in CKD Patients with Pulmonary Hypertension A Retrospective Study. BMC Nephrology, 19(1): 70–77.

[7] Tang M, Batty JA, Lin C, et al., 2018, Pulmonary Hypertension Mortality and Cardiovascular Disease in CKD and ESRD Patients: A Systematic Review and Meta Analysis. American Journal of Kidney Diseases, 72(1): 75–83.

[8] Thenappan T, 2017, Pulmonary Hypertension in Chronic Kidney Disease: A Hemodynamic Characterization. Pulmonary Circulation, 7(3): 567–568.

[9] Jaroszyński A, Schlegel TT, Zaborowski T, et al., 2022, The Value of Ventricular Gradient for Predicting Pulmonary Hypertension and Mortality in Hemodialysis Patients. Scientific Reports, 12(1): 456–464.

[10] Humbert M, Gerry Coghlan J, Khanna D, 2012, Early Detection and Management of Pulmonary Arterial Hypertension. European Respiratory Review, 21(126): 306–312.

[11] Qin J, Wang G, Han D, 2023, Benefits of Macitentan in Patients with Pulmonary Hypertension: A Systematic Review and Meta Analysis of Randomized Controlled Trials. Global Heart, 18(1): 58–58.

[12] Pradhan A, Tyagi R, Sharma P, et al., 2024, Shifting Paradigms in the Management of Pulmonary Hypertension. European Cardiology Review, 19: e25–e25.

[13] Chin KM, Sitbon O, Doelberg M, et al., 2021, Three Versus Two Drug Therapy for Patients with Newly Diagnosed Pulmonary Arterial Hypertension. Journal of the American College of Cardiology, 78(14): 1393–1403.

[14] Li J, Yang ZY, Wang S, et al., 2022, Efficacy and Safety of Switching from Bosentan or Ambrisentan to Macitentan in Pulmonary Arterial Hypertension: A Systematic Review and Meta Analysis. Frontiers in Cardiovascular

Medicine, 9: 977110–977110.

[15] Du D, Yuan YD, 2023, Efficacy and Safety of Macitentan for Pulmonary Hypertension: A Meta Analysis. The Clinical Respiratory Journal, 17(11): 1117–1129.

[16] Walther CP, Nambi V, Hanania NA, et al., 2020, Diagnosis and Management of Pulmonary Hypertension in Patients with CKD. American Journal of Kidney Diseases, 75(6): 935–945.

[17] Kim NH, Chin KM, McLaughlin VV, et al., 2025, Macitentan and Tadalafil Combination Therapy in Patients with Pulmonary Arterial Hypertension and Cardiovascular Comorbidities Real World Evidence from OPUS and OrPHeUS. Advances in Therapy, 42(7): 3306–3333.

[18] Zebadúa R, Hernández-Pérez AP, García A, et al., 2021, Macitentan in the Treatment of Pulmonary Arterial Hypertension. Future Cardiology, 17(1): 49–58.

[19] Bedan M, Grimm D, Wehland M, et al., 2018, A Focus on Macitentan in the Treatment of Pulmonary Arterial Hypertension. Basic and Clinical Pharmacology and Toxicology, 123(2): 103–113.

[20] Wang G, Qin J, Han D, 2023, Long Term Safety of Macitentan in Patients with Pulmonary Hypertension: A Meta Analysis of Randomised Controlled Trials. European Journal of Clinical Investigation, 53(11): e14059–e14059.