doi:10.22100/ijhs.v12i2.1261
Original Article

SJMS 2026;12(2):19-23
sjms.shmu.ac.ir

SJMS
Shahroud Journal of Medical Sciences

The Effect of Improved Hemodialysis Adequacy on Primary Pulmonary Hypertension in End Stage Renal Disease Patients

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Received: 28 May 2025
Accepted: 22 October 2025

Abstract

Background: *Hemodialysis serves as a vital life-support therapy that balances electrolytes and fluid levels while eliminating toxic substances from the body, thereby enabling patient survival. Enhanced dialysis efficacy is directly linked to a reduction in uremic complications and a decrease in mortality rates. Pulmonary hypertension (PH) represents a progressive condition stemming from cardiovascular, pulmonary, or systemic disorders, which is characterized by elevated morbidity and death risks. It is hypothesized that optimizing the quality of dialysis may mitigate PH. Consequently, this research was designed to assess how enhancing dialysis adequacy impacts pulmonary artery pressure (PAP) in hemodialysis patients residing in Shahroud.*

Methods: *Employing a descriptive-analytic and longitudinal design, this study was carried out in 2023 at Imam Hossein Hospital, Shahroud, involving patients undergoing hemodialysis. Initially, an expert cardiologist utilized two-dimensional color Doppler echocardiography to determine systolic PAP. These measurements were taken the day following a dialysis session. Additionally, metrics regarding dialysis adequacy were documented for all participants. Subsequently, after a six-month interval during which specific interventions were implemented to boost dialysis adequacy, the patients underwent a repeat echocardiographic evaluation. The resulting PAP values were then analyzed and compared with the baseline data.*

Results: *The study cohort comprised 55 individuals, among whom 37 achieved adequate dialysis levels, while 18 were categorized as having insufficient dialysis. The average age of the participants was 56.62±16.78 years, a figure that remained statistically consistent across the groups. In terms of gender distribution, the population included 32 males (58.2%) and 23 females (41.8%). The overall mean PAP was recorded at 30±13 mmHg. Specifically, 28 subjects (50.9%) exhibited normal PAP levels, whereas the remaining 27 (49.1%) presented with elevated pressure. At the baseline assessment, 15 patients (83.3%) within the insufficient dialysis group demonstrated increased PAP. However, by the conclusion of the study—and following interventions to optimize dialysis adequacy—this number decreased to 12 patients (66.7%), representing a statistically significant reduction (P-value=0.001).*

Conclusion: *The findings indicate that enhancing the adequacy of dialysis leads to a substantial reduction in PAP and contributes to the improvement of the quality of life for patients undergoing hemodialysis.*

Keywords: Hemodialysis, Pulmonary hypertension, Dialysis adequacy.
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Please cite this paper as: Rashidi S, Amerian M, Rafiee H, Pourmand K, Taherian N, Ariya S, Sohrabi MB. The Effect of Improved Hemodialysis Adequacy on Primary Pulmonary Hypertension in End Stage Renal Disease Patients. Shahroud Journal of Medical Sciences 2026;12(2):19-23.

Introduction

Chronic Kidney Disease (CKD) is characterized by a permanent and progressive deterioration of renal tissue, eventually resulting in end-stage renal failure[1]. For survival, affected individuals depend on renal replacement therapies, including dialysis and transplantation[2]. While the prevalence of specific treatments varies by location, hemodialysis remains the predominant modality globally[3]. In Iran specifically, approximately 25,600 patients across 375 centers are currently receiving chronic hemodialysis, a figure that grows by roughly 8% annually[4, 5]. Patients undergoing dialysis face a wide array of physical and psychological challenges. Suboptimal dialysis efficacy leads to poor control of blood toxins, thereby elevating both morbidity and mortality risks[4, 5]. Extensive research by the National Dialysis Association demonstrates a direct correlation between higher dialysis quality and reduced uremic complications and death rates[6]. Furthermore, the adequacy of dialysis serves as a critical predictor for hospitalization and mortality[7]. The standard measure for dialysis adequacy, KT/V, is established at 1.8 for twice-weekly sessions and 1.2 for thrice-weekly sessions; failing to meet these thresholds exacerbates uremic issues[8]. Notably, individuals with a KT/V below 0.8 experience significantly higher rates of complications and hospitalizations compared to those with values ranging from 0.8 to 1.4[8, 9].

Pulmonary hypertension (PH) is a progressive condition stemming from cardiovascular, pulmonary, or systemic pathologies. Regardless of the underlying cause, PH is linked to heightened complications[10]. Reported prevalence rates among dialysis populations vary widely, falling between 20% and 58% across different studies[11]. The etiology of PH in this group is multifactorial, encompassing left ventricular failure, pulmonary artery calcification due to hyperparathyroidism, elevated cardiac output from arteriovenous fistulas, anemia, and fluid overload[11, 12]. A diagnosis of PH is confirmed when the pulmonary artery systolic pressure exceeds 35 mmHg[13].

Currently, Doppler echocardiography allows for the non-invasive and accurate measurement of pulmonary artery pressure (PAP) in the majority of patients[14]. Early diagnosis enables the treatment of root causes prior to the onset of right ventricular failure, thereby mitigating severe and potentially

irreversible complications[14, 15]. Given the diverse origins of PH in hemodialysis patients, its profound effect on quality of life, and the scarcity of precise data regarding how dialysis adequacy influences PH incidence, this study was designed to evaluate the impact of enhancing dialysis quality on primary PH in hemodialysis patients within Shahroud.

Materials and Methods

This investigation employed a descriptive-analytic design with a longitudinal approach, involving hemodialysis patients at Imam Hossein Hospital in Shahroud. The study was conducted over a period spanning from March 2022 to December 2023.

Inclusion and Exclusion Criteria: Eligibility for participation required individuals to be over 18 years of age, undergoing routine hemodialysis for a minimum of three months, and receiving at least two dialysis sessions per week. Additional requirements included the absence of emergency dialysis needs, stable vital signs, and a voluntary willingness to partake in the research.

Patients were excluded based on several factors: advanced malignancies; moderate to severe left ventricular failure (defined as left ventricular EF<40%); significant mitral or aortic valve disease; severe cerebrovascular or chronic liver conditions; chronic obstructive pulmonary disease (COPD); and a history of pulmonary embolism. Furthermore, exclusion criteria encompassed interstitial lung disease, collagen vascular disorders such as systemic lupus erythematous (SLE), smoking, obstructive sleep apnea, and congenital left-to-right shunts. Participants who chose to withdraw or expressed regret at any phase of the study were also excluded.

Sample Size: The sample size was determined using relevant statistical formulas, taking into account the hemodialysis population of Shahroud and the objectives of the study. Consequently, 60 eligible hemodialysis patients were selected using a convenience sampling method. It is important to note that five patients were unable to complete the study due to deterioration in their clinical condition, resulting in a final sample size of 55 patients.

Participants were recruited using a convenience sampling method. Enrollment followed a comprehensive explanation of the research objectives and the acquisition of informed consent from all subjects.

Measurement of PAP: On the day following a dialysis session, systolic PAP was assessed by a skilled cardiologist utilizing a General Electric (GE) echocardiography system. Each patient underwent a two-dimensional color Doppler echocardiographic examination. The systolic velocity of tricuspid regurgitation was measured via apical or parasternal views. Subsequently, systolic pulmonary artery pressure (SPAP) was calculated using the modified Bernoulli equation:

PAP=4×(tricuspid systolic jet)^2+10 mmHg (representing estimated right atrial pressure)

In this study, an SPAP exceeding 35 mmHg was established as the diagnostic threshold for PH[16, 17]. Based on this parameter, the cohort was stratified into two distinct groups: those with PH (>35 mmHg) and those without PH (≤35 mmHg)[13].

Assessment of Dialysis Adequacy: Participants were further categorized according to the quality of dialysis. Patients with a KT/V<1.2 were classified as having dialysis insufficiency, whereas those with a KT/V≥1.2 were categorized as having adequate dialysis[18].

Intervention and Follow-up: Initially, dialysis adequacy was evaluated across the cohort to identify the causes of any insufficiency. Subsequently, specific strategies were implemented to enhance dialysis quality. These measures included verifying procedural issues related to dialysis failure, assessing vascular access function, and optimizing parameters such as hemodialysis duration, frequency, and blood flow rate. Additionally, the management of intradialytic hypotension, confirmation of sufficient anticoagulation, proper filter placement, strict regulation of antihypertensive medications, and anemia management were carried out.

All participants were monitored for a six-month period, during which the aforementioned interventions were applied to optimize dialysis adequacy. At the end of this interval, patients underwent a repeat echocardiographic examination to reassess the severity of SPAP. Finally, the data obtained from the baseline and post-intervention assessments were compared.

Statistical Analysis and Ethics: prior to participation, informed consent was obtained from all individuals involved. Data were recorded electronically and analyzed using SPSS software, version 23. The analysis employed descriptive statistics, including frequency, mean, and standard deviation (Mean±SD), as well as analytical tests such as the chi-square and t-test. Ethical approval for this research was granted by the Institutional Review Board of Shahroud University of Medical Sciences (IR.SHMU.REC.1403.036), in compliance with the Declaration of Helsinki.

Results

Among the 55 participants included in the study, 37 achieved adequate dialysis, while 18 were classified as having insufficient dialysis. The mean age of the entire cohort was 56.62±16.78 years. Regarding gender distribution, 23 patients (41.8%) were female and 32 (58.2%) were male. Diabetes mellitus was identified as the leading cause of renal failure, accounting for 27 cases (49.1%).

Table 1 presents the findings regarding personality traits, as well as clinical and paraclinical characteristics of the patients.

Table 1. The results of the demographic, clinical and para clinical factors of the patients

Variable	Mean±SD or Number (%)
Sex	
Male	32 (58.2)
Female	23 (41.8)
Average dialysis duration (years)	3.61±1.43

Dialysis duration group (years)	
≤2	22 (40.0)
>2	33 (60.0)
Dialysis adequacy group (liters)	
Good	37 (67.3)
Poor	18 (32.7)
Average age of patients (years)	56.62±16.78
Average BMI of patients (kg/m2)	24.38±3.91
Average dialysis duration per session (hours)	
≤3	37(67.3)
>3	18(32.7)
Cause of ESRD	
Hypertension	18 (32.7)
Diabetes mellitus	27 (49.1)
Others	10 (18.2)

The mean PAP across the study population was recorded at 30±13 mmHg. Specifically, 28 patients (50.9%) exhibited normal PAP (≤35 mmHg), whereas 27 patients (49.1%) presented with elevated PAP (>35 mmHg). At the baseline assessment, 15 patients (83.3%) within the insufficient dialysis group demonstrated elevated PAP. However, by the conclusion of the study following interventions to correct dialysis insufficiency this number decreased to 12 patients (66.7%). This reduction was found to be statistically significant (P-value=0.001). Table 2 illustrates the correlation between the enhancement of dialysis quality and the resultant improvement in PAP.

Table 2. Investigating the relationship between improving dialysis quality and improving pulmonary artery pressure

	Beginning of the study Mean± SD or Num (%)	End of the study Mean± SD or Num (%)	P-value
Average dialysis adequacy	0.998±0.203	1.140±0.148	0.001
Dialysis adequacy			
Good	0 (0)	10 (55.6)	0.001
Poor	18 (100)	8 (44.4)	
Average Pulmonary artery pressure	37.42±8.33	35.66±9.18	0.030
Pulmonary artery pressure			
≤35	3 (16.7)	6 (33.3)	0.001
>35	15 (83.3)	12 (66.7)	

Discussion

The outcomes of our investigation demonstrate that enhancing dialysis adequacy leads to a notable reduction in PAP (P-value=0.001). This result aligns substantially with the findings reported by Galie and Bussone[19, 20].

Inadequate dialysis serves as a critical determinant of both physical and psychological ailments in this population; conversely, optimizing adequacy is crucial for enhancing their quality of life[21]. PH is defined as a relatively rare condition characterized by the thickening and stiffening of pulmonary arterial walls, which impedes sufficient blood flow[22]. This pathology predominantly affects young adults aged 30 to 40 and exhibits a higher prevalence in females. The progressive nature of the disease often culminates in right heart failure and severe dyspnea. Primary PH is considered rare, with an estimated incidence of 2 to 3 cases per million people, though it can also occur in children; it is three times more common in women than in men. Epidemiologically, approximately 90-95% of PH cases are classified as secondary, while only 5-10% are primary[22-24].

In the research conducted by Caughey et al., it was observed that enhancing dialysis adequacy had a beneficial impact on right ventricular function. Although a reduction in PAP was noted in their study, it did not reach statistical significance. Nevertheless, this finding remains largely comparable to the results of the present investigation[25].

Similarly, Joannidis et al., indicated that boosting dialysis efficiency resulted in improved cardiac indices for patients, alongside relative improvements in laboratory markers such as hemoglobin and phosphorus levels. These observations are partially consistent with the data obtained in our study[26].

Dialysis adequacy stands out as one of the most significant variables influencing the quality of life for hemodialysis patients. Primary contributors to dialysis insufficiency include suboptimal dialysis dosing, patient-specific issues (such as hypotension and symptoms during dialysis), and technical variables (including equipment type, operational speed, and filter specifications)[27, 28].

A study by Navaneethan et al., highlighted the efficacy of dialysis adequacy in stabilizing the vital signs of hemodialysis patients. Specifically, it plays a role in maintaining cardiac

parameters, including right ventricular pressure and PAP, within optimal ranges[29].

Rabih et al., emphasized that ensuring dialysis adequacy is not a subjective matter for most patients; rather, interventions such as adjusting dialysis duration, managing blood pressure, and selecting appropriate filters can prove effective and beneficial in this regard[30].

Administering dialysis that is both accurate and calculated, accompanied by rigorous monitoring of influencing factors, can prevent numerous complications. By minimizing the need for recurrent hospitalizations, this approach not only reduces medical costs but also fosters a superior quality of life and potentially extends survival for dialysis patients[31, 32].

Furthermore, by closely tracking dialysis adequacy and evaluating all determinants of this metric, it is feasible to enhance the well-being of patients and substantially lower the burden of associated complications such as cardiovascular and respiratory disorders as well as mortality rates[31-33].

Research by Wang et al., revealed that while dialysis adequacy remains suboptimal in more than half of the hemodialysis population, efforts to improve it can significantly attenuate cardiovascular and pulmonary complications[34].

Jin et al., noted that the pattern of pulmonary arterial hypertension in hemodialysis patients is variable. They stressed the necessity of optimizing the dialysis process, particularly adequacy, to mitigate complications and mortality[35]. The conclusions of both Wang and Jin regarding the critical role of optimal dialysis adequacy in reducing morbidity and mortality are fully congruent with our findings, underscoring the need for diligent monitoring of this parameter in these patients[34, 35].

Conclusions: This study demonstrates that enhancing dialysis adequacy leads to a substantial reduction in PAP and significantly improves the quality of life for hemodialysis patients. Consequently, it is imperative to assess and strictly manage all determinants of dialysis adequacy to mitigate morbidity and mortality rates in this patient population.

Limitations: This research faced sample size constraints resulting from patient mortality, the withdrawal of participants, and unstable clinical conditions that precluded continued involvement for some subjects. Consequently, it is recommended that future investigations be conducted with a larger cohort and preferably employ a multicenter design.

Ethical Considerations

This article is the result of the thesis for the degree of Doctor of Specialty Medicine, which has been registered with the Ethics Committee of Shahroud University of Medical Sciences under the ethics code (IR.SHMU.REC.1403.036). Oral and written consent was obtained from the patients. No additional costs were imposed on them and their right to withdraw from the study was guaranteed.

Acknowledgment

This research was conducted as a Medical Doctor (MD) thesis with the support of Shahroud University of Medical Sciences. We hereby express our gratitude to the Research Deputy for their assistance.

Conflict of Interest

The authors declare that they have no conflicts of interest.

Funding

Financial support for this research was provided by the Vice-Chancellor for Research of Shahroud University of Medical Sciences.

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