



## Comparison of pulmonary arterial pressure in patients under chronic hemodialysis with and without arteriovenous fistula

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### Original Article

#### Abstract

**BACKGROUND:** Pulmonary arterial hypertension (PAH) is a progressive disorder and a newly-discovered disease in people with end stage renal disease (ESRD). In patients who are hemodialyzed through arteriovenous fistula (AVF), the incidence of pulmonary hypertension (PHT) is highly probable. Regarding the main role of the AVF in the pathogenesis of PAH and the fact that AVF is the main method of vascular access in patients undergoing dialysis, we decided to investigate pulmonary artery pressure (PAP) in patients under chronic hemodialysis.

**METHODS:** This was a cross-sectional study. All patients with chronic hemodialysis were divided into two groups according to the status of the fistula. The number of cases examined included 100 patients and data were analyzed by SPSS software.

**RESULTS:** The most common cause of ESRD was hypertension (HTN) followed by diabetes mellitus (DM), polycystic kidney disease (PKD), urologic disorders, DM and HTN, combined blood pressure (BP) and PKD, renal stones, and other items ultimately. The average creatinine level was 8.59 mg/dl. Therefore, the mean creatinine level of patients, although relative to mode and median, was in any case significantly higher than the mean, which was predictable according to the ESRD community studied. The mean phosphate level was 5.66 mg/dl, and the mean hemoglobin (Hb) was 11.56 g/dl. The mean parathyroid hormone (PTH) and PAP were 558.68 and 27.33 mmHg, respectively, and the mean of ejection fraction (EF) was 50.75%. There was a significant difference between the mean PAP in the two groups ( $P = 0.048$ ), as it was higher in the AVF group.

**CONCLUSION:** Results of this study showed that AVF and ESRD both were risk factors for high PAP and PHT.

**KEYWORDS:** Pulmonary Hypertension, End Stage Renal Disease, Arteriovenous Fistula

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#### Introduction

Pulmonary artery hypertension (PAH) is a progressive disorder that regardless of its cause of the illness can complicate cardiac, pulmonary, and systemic diseases and also can cause an increase in mortality rate.<sup>1</sup> PAH is a newly-discovered disease in end stage renal

disease (ESRD).<sup>2</sup> In patients who are hemodialyzed with arteriovenous fistula (AVF), the incidence of pulmonary artery pressure (PAP) is highly probable.<sup>3</sup> Recently, the prevalence of PAH in patients with ESRD is about 40%-50%<sup>4</sup> and in Iran, it is estimated to be 29%-66%.<sup>5-9</sup> The normal systolic blood pressure (SBP) of the pulmonary artery is 30 mmHg.<sup>10</sup> PAP is supposed to be the systolic PAP of more than 35 mmHg in resting

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position, which is estimated by Doppler echocardiography.<sup>11</sup> This increase in pressure can be due to cardiac, pulmonary, or systemic disorders.<sup>4,12</sup> AVF is the gold standard for hemodialysis, with a success rate of about 84%, which is designed to improve the effectiveness of hemodialysis.<sup>13</sup> The prevalence of AVF in American hemodialysis patients is 60.2%.<sup>14</sup> A good functional AVF is a device that provides a blood flow equivalent to 350-400 ml/min.<sup>15</sup> When chronic kidney disease (CKD) progresses to ESRD, renal replacement therapy (RRT) is essential for survival, and hemodialysis is the most common form of treatment.<sup>16</sup> Cardiovascular events are the cause of most deaths in patients with ESRD.<sup>17</sup> A strong direct relationship between PAP and age, duration of dialysis treatment, urea, blood creatinine, phosphate, and serum parathyroid hormone (PTH) levels, cardiac outflow, and AVF current (which is associated with anemia and increased fluid burden) and an inverse relationship between PAP and serum bicarbonate and ejection fraction (EF) have been reported in patients undergoing hemodialysis.<sup>4</sup> The size and location of AVF are also involved in the PAP enhancement mechanism.<sup>18</sup> PAH improves after renal transplantation, as well as after short AVF compression, which indicates the pathogenicity of ESRD and AVF in PAH.<sup>19</sup> In hemodialysis patients with PAH, there is a significant increase in cardiac output compared with patients without PAP.<sup>4</sup> Right ventricular SBP (RVSBP) more than 50 mmHg is related with a significant reduction in survival after transplantation<sup>20</sup> and the duration of hemodialysis has a strong correlation with RVSBP increase.<sup>21</sup> In fact, ESRD increases the risk of death and cardiovascular disease (CVD) and increases the need for special health care.<sup>22</sup> In clinical experience, blood shunt from right to left and increased pulmonary blood flow (PBF) are common side effects of PAH.<sup>23</sup> PAH can have

adverse effects on the quality of life of patients, which is usually very overwhelming.<sup>24</sup> Kidney transplantation significantly reduces the PAP level and makes it close to the normal range.<sup>4</sup> In this study, we try to compare the PAP in patients on dialysis with and without AVF in Tohid Hospital, Sanandaj, Iran, during 2016.

## Materials and Methods

This cross-sectional study was conducted on patients with ESRD undergoing hemodialysis in Tohid Hospital in Sanandaj City during 2016. The criteria for entering the study were all people over the age of 18 who have been undergoing hemodialysis for at least 6 months, and the exclusion criteria were the hemodialysis patients under the age of 18 years, hemodialysis patients who had undergone less than 6 months of their dialysis, those with uncontrolled BP (mean BP more than 160/100 mmHg before study entry), pregnancy, and recent malignancy. All patients with chronic hemodialysis were studied in the dialysis ward of Tohid Hospital in Sanandaj, which were 100 people. Patients were classified into two groups according to the status of the fistula. Exposure group (I) was a group of people who used AVF for dialysis, and a non-exposed group (II) was a group of people who used non-AVF method for dialysis (a permanent, temporary, or graft catheter). The case group was divided into three subgroups based on the duration of dialysis:

A: Less than 12 months since the start of their dialysis

B: Between 12-24 months since the start of their dialysis

C: Over 24 months since the start of their dialysis

For both groups, a questionnaire was administered including age, sex, cause of ESRD, history of smoking, duration of dialysis, the presence or absence of AVF, the site of AVF (brachialis or radialis), urea, creatinine, phosphate, PTH, and hemoglobin (Hb) levels

as well as the result of echocardiography, all of which were available in patients' files and were extracted from the patients' files and examination by the student, that the questionnaire was completed based on it (access to patient file information was taken from them). Echocardiography was performed by a cardiologist after a dialysis session to determine PAP for all patients. Basic characteristics and echocardiography variables (EF, PAP) were compared in both groups. Data were entered into SPSS software (version 24, IBM Corporation, Armonk, NY, USA) and analyzed by a statistical consultant for statistical analysis. Descriptive goals were quantitatively calculated with a few statements such as mean, median, faces, and tables showing graphs. For quantitative analytical purposes, the default normality was calculated by t-test and otherwise calculated with non-parametric sampling. Qualitative analytical objectives were calculated using qualitative methods such as logistic regression.

## Results

**Descriptive results:** In this study, 100 patients were examined, that all of them (100%) were valid. Patients with AVF (positive group) included 66 patients (66%), and 34 (34%) patients did not have the fistula. 60% of patients were older than 60 years old and 40%

of them aged less than 60 years. 54% of the patients were men and 46% were women. 9% of them had a history of smoking, and 91% had no history of smoking.

**Table 1. Frequency distribution of causes of end stage renal disease (ESRD) in cases under study**

Patients comorbidities	n (%)	Valid percent	Cumulative percent
Valid			
DM	7 (7.0)	7.1	7.1
HTN	66 (66.0)	67.3	74.5
DM and HTN	4 (4.0)	4.1	78.6
PKD	6 (6.0)	6.1	84.7
HTN and PKD	3 (3.0)	3.1	87.8
Urologic disorders	6 (6.0)	6.1	93.9
Renal stone	3 (3.0)	3.1	96.9
Other	3 (3.0)	3.1	100
Total	98 (98.0)	100	
Missing System	2 (2.0)		
Total	100 (100)		

DM: Diabetes mellitus; HTN: Hypertension; PKD: Polycystic kidney disease

Table 1 lists the causes of ESRD in which major causes including diabetes mellitus (DM), hypertension (HTN), DM and BP, polycystic kidney disease (PKD), PKD and HTN, urological disorders, and renal stone problems as well as other factors are calculated. The most common cause of ESRD in the current study was HTN with 66% of cases, followed by DM, PKD, urologic disorders, DM and HTN, combined BP and PKD, renal stones, and other items ultimately.

**Table 2. Mean and standard deviation (SD) of quantitative variables in the cases**

Analytic parameters	Age (year)	Urea (mg/dl)	Creatinine (mg/dl)	Phosphate (mg/dl)	Hb (mg/dl)	PTH (Pg/m)	PAP (Pg/m)	EF (%)	
Number	Valid	100.00	100.00	100.00	100.00	100.00	98.00	85.00	93.00
	Missing	0	0	0	0	2.00	15.00	7.00	
Mean		60.75	78.07	8.59	5.66	11.56	558.68	27.33	50.75
Median		60.50	69.00	7.50	5.10	11.50	380.00	20.00	52.00
Mode		60.00	60.00	9.30	5.10	10.50	380.00	15.00	60.00
SD		13.26	72.12	8.59	4.76	1.68	508.69	14.28	11.04
Variance		175.98	5202.49	73.88	22.68	2.82	258775.06	204.02	122.03
Skewness		-0.04	7.30	8.15	8.87	0.90	1.82	1.03	-1.38
SES		0.24	0.24	0.24	0.24	0.24	0.24	0.26	0.25
Minimum		26.00	23.00	1.80	3.00	8.40	26.00	4.50	10.00
Maximum		94.00	711.00	88.00	51.00	19.30	2400.00	70.00	65.00
Percentiles	25	53.25	55.00	5.82	4.20	10.50	210.00	15.00	45.00
	50	60.50	69.00	7.50	5.10	11.50	380.00	20.00	52.00
	75	69.75	80.00	9.30	6.25	12.80	720.00	37.00	60.00

Hb: Hemoglobin; PTH: Parathyroid hormone; PAP: Pulmonary artery pressure; EF: Ejection fraction; SD: Standard deviation; SES: Standard error of skewness

Table 2 is the most important table for the present study. This table explores all the variables studied in this study. In the case of age, the average age of the subjects was  $60.75 \pm 13.26$  years. The mean of urea was  $78.07 \pm 72.12$ . In the case of creatinine, the average creatinine level of 100 patients tested was 8.59 mg/dl. Therefore, the mean creatinine level of patients, although relative to mode and median, was in any case significantly higher than the mean, which is predictable according to the ESRD community studied. The average phosphate in the 100 patients examined was 5.66 mg/dl, and the mean Hb in 100 patients was 11.56. The mean PTH and PAP in 98 patients examined were 558.68 and 27.33 mmHg, respectively, and the EF mean for 100 patients was 50.75%.

**Analytical results:** T-test showed that there was no significant difference between the mean and standard deviation (SD) of quantitative variables in the two groups ( $P > 0.05$ ). There was a significant difference between the mean PAP in the two groups ( $P = 0.04$ ), as it was higher in the AVF group. Analysis of chi-square test showed no significant difference between the duration of dialysis period in patients with chronic hemodialysis in the two groups ( $P = 0.04$ ).

## Discussion

PAH is a progressive disorder that causes cardiovascular, pulmonary, or systemic diseases and mortality, irrespective of its cause.<sup>1</sup> This study was conducted on 100 patients with chronic dialysis in dialysis ward of Tohid Hospital in Sanandaj City, in 2016, in terms of the fistula in one of two groups, to determine the average PAH in chronic hemodialysis patients with and without AVF. In this study, patients with AVF (positive group) included 66 patients (66%), and 34 (34%) patients did not have the fistula. 60% of patients were older than 60 years old and 40% of them aged less than 60 years. 54% of the patients were men and 46% were women. 9% of them had a history of smoking,

and 91% had no history of smoking.

Recently, the incidence of pulmonary hypertension (PHT) in patients with ESRD is estimated as 40%-50%.<sup>4</sup> The most important causes of ESRD in the cases studied are DM, HTN, DM and HTN, PKD, HTN and PKD, urological problems, and renal stones. The most common cause of ESRD in the current study was HTN with 66% of cases, followed by DM, PKD, urologic problems, DM and HTN, HTN and PKD, renal stones, and other items ultimately. High BP also increases the risk of hemorrhage from the fistula, in addition to the high BP side effects, and increases the risk of falling. Low BP results in blood thrombosis and fistula disruption due to a decrease in blood flow. In this study, the mean urea was  $78.07 \pm 72.12$ . In the case of creatinine, the average creatinine level of 100 patients tested was 8.59 mg/dl. Therefore, the mean creatinine level of patients, although relative to mode and median, is in any case significantly higher than the mean, which is predictable according to the ESRD community studied. The average phosphate in 100 patients examined was 5.66 mg/dl, and the mean Hb in 100 patients was 11.56 g/dl. The mean PTH and PAP in 98 patients examined were 558.68 and 27.33 mmHg, respectively, and the EF mean for 100 patients was 50.75%. Analytical results of this study showed that there was no significant difference between the mean and SD of quantitative variables in the two groups ( $P > 0.05$ ). There was a significant difference between the mean PAP in the two groups ( $P = 0.04$ ), as it was higher in the AVF group. Analysis of chi-square test showed no significant difference between the duration of dialysis period in chronic hemodialysis patients in the two groups ( $P = 0.04$ ).

In a study conducted by Hayati et al., 60 patients undergoing hemodialysis were divided into two groups exactly like the present study. In group 1, PAP was higher than group 2 ( $P < 0.05$ ). PHT was 86.64% and

0% in group 1 and 2, respectively ( $P < 0.05$ ). Also, in comparing PAP prevalence in two groups, similar results were obtained in hands. It was concluded that higher PAP was associated with a higher incidence of PHT ( $P < 0.01$ ). PAP and PHT were significantly higher in patients with ESRD undergoing continuous hemodialysis with AVF. Therefore, AVF was a predictive factor for a higher PAP and an increase in the incidence of PHT in hemodialysis patients,<sup>25</sup> which is somewhat similar to the results of our study. In a study by Acarturk *et al.*, 32 patients under hemodialysis participated in the study, with a median time of  $32.7 \pm 34.1$  months to build a fistula. Anatomical location was vascular dysentery in 24 radial patients and in 8 brachial patients. There was a correlation between mean PAP and cardiac index ( $r = 0.45$ ,  $P = 0.01$ ), but other variables such as AVF, calcium phosphate, PTH activity, fistula location, fistula formation time, and PAP were not significantly associated. In 14 patients (43.7%), PHT was diagnosed. Variables were compared between patients with and without PHT. Patients with PHT had a significantly higher cardiac index ( $P = 0.03$ ), but there was no significant difference between the other variables. The mean PAP was found to be related to the cardiac index ( $P = 0.01$ ). However, no relation was found between mean PAP and AVF, Hb, calcium-phosphorus, and PTH levels ( $P = 0.03$ ).<sup>3</sup> In a study by Hemnes *et al.*, 91 patients were divided into two groups: dialysis patients with PHT (40 patients) and without PHT (51 patients). The duration of dialysis was  $40.5 \pm 47.0$  months. DM, HTN, or both were the most common causes of ESRD (54%). Of the 91 patients, 29 patients (32%) had hemodialysis by the catheter. 41 patients (45%) had AVF and 21 patients (23%) had AV grafts. The mean dialysis time in the AV graft or AVF group was not different from that of the catheter dialysis group ( $P = 0.24$ ). There was no

difference in age, sex, and race in patients with PHT and those without PHT. Patients with PHT were more likely to have long-term hemodialysis with an average of  $52.6 \pm 58.2$  months. However, in patients without fistula, it was  $31.0 \pm 33.7$  hours ( $P = 0.02$ ). In patients with PHT, the mean serum phosphate level ( $P = 0.04$ ) and calcium ( $P = 0.50$ ) was lower, but the PTH level was higher ( $P = 0.40$ ) than the other group, but it was not very significant. However, lower levels of creatinine were significant ( $P = 0.04$ ).<sup>26</sup>

### Conclusion

PAH is a progressive disorder and a newly-discovered disease in people with ESRD. In patients who are hemodialyzed through AVF, the incidence of PHT is highly probable. Regarding the main role of the AVF in the pathogenesis of PAH and the fact that AVF is the main method of vascular access in dialysis patients, we decided to investigate PAP in patients with chronic hemodialysis. The number of cases examined included 100 patients. It is the biggest sample in this topic until now. The most common cause of ESRD was HTN followed by DM, PKD, urologic disorders, DM and HTN, combined BP and PKD, renal stones, and other items ultimately. There was a significant difference between the mean PAP in the two groups ( $P = 0.04$ ), as it was higher in the AVF group. Finally, our study showed that AVF and ESRD both were risk factors for high PAP and PHT. Of course, to confirm this hypothesis, we need a larger sample size and finally meta-analysis.

### Conflict of Interests

Authors have no conflict of interests.

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