

## Effect of Pulmonary Hypertension Severity on Graft Function and Quality of Life after Transplantation in Patients with End-Stage Renal Disease

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ARTICLE INFO	ABSTRACT
<p><b>Article type:</b> Original Article</p> <hr/> <p><b>Article History:</b> <b>Received:</b> 17-Nov-2021 <b>Accepted:</b> 26-Jan-2022</p> <hr/> <p><b>Key words:</b> End-stage kidney failure, Kidney transplantation, Pulmonary hypertension, Quality of life</p>	<p><b>Introduction:</b> The present study aimed to assess the effect of pulmonary hypertension (PH) severity on the quality of life after transplantation in patients with end-stage renal disease (ESRD).</p> <p><b>Materials and Methods:</b> In this cohort study, 60 ESRD patients who underwent kidney transplantation were followed for at least one year. Basic and laboratory findings were recorded in patients before and after transplantation. Quality of life was assessed by the 12-item health-related quality of life questionnaire (SF-12). The severity of PH was assessed based on pulmonary artery systolic pressure (PASP), and severe cases were excluded from the study. The obtained data were analyzed in SPSS software (version 24) using the chi-square test, independent t-test, and Pearson's correlation.</p> <p><b>Results:</b> Based on the results, PH was observed in 83.3% of patients before transplantation. Following transplantation, there was a significant increase in quality of life and glomerular filtration rate (GFR) (P=0.001). Patients with PH had a lower quality of life before transplantation, as compared to those without PH (P= 0.009). Furthermore, the PASP level showed a significant positive relationship with the age of patients (r= 0.465; P&lt;0.001) and the rate of improvement in quality of life after transplantation (r=0.288; P= 0.02).</p> <p><b>Conclusion:</b> As evidenced by the results of this study, kidney transplantation improves kidney function and the quality of life of patients. The presence of PH leads to lower quality of life in ESRD patients before transplantation but has no effect on it after transplantation. Moreover, the severity of PH had no effect on the outcomes of a kidney transplant.</p>
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## Introduction

End-stage renal disease (ESRD) is a serious disease with adverse consequences and high medical costs (1). Its prevalence is increasing in developing countries, such as Iran, as well as other parts of the world (2). In Iran, 50% of these patients undergo hemodialysis (3). Kidney transplantation improves the quality of life in these patients and improves the survival rate in some patients (2). Cardiovascular disease is the leading cause of death in patients with chronic kidney disease (CKD) (4). Pulmonary hypertension (PH) is a cardiovascular complication in CKD, especially in ESRD patients. The prevalence of PH in patients with ESRD varies from 27%-58% (5). The PH is often progressive after development and an independent determinant of increased mortality in patients with CKD (5-6).

Kidney transplantation is performed in patients with mild to moderate PH (10-11), and severe PH is associated with decreased post-graft survival and increased post-graft cardiovascular complications (12-13). Despite the high prevalence of PH in ESRD patients undergoing kidney transplantation, there is a dearth of information on post-transplant consequences in patients with mild to moderate PH before transplantation. In one of these few studies, it was stated that mild to moderate PH before transplantation had no effect on transplant consequence and death over a four-year period. Nonetheless, a higher PH results in a more dramatic decrease in estimated Glomerular Filtration Rate (eGFR) in the first and second years after transplantation (14). The association of PH with renal dysfunction and increased mortality in dialysis patients has recently come into the focus of researchers. It seems to exert an effect on the treatment and prognosis of kidney patients; nonetheless, there is no general consensus on the prognostic effect of PH on transplanted kidney function. The role of pulmonary hypertension in post-transplant consequences has been evaluated and yielded different results. Some studies have suggested that the presence of pulmonary hypertension caused heart changes, delayed kidney function, and

decreased life expectancy (15-17); however, no effect was observed in another study (18).

Some studies have suggested that the presence of pulmonary hypertension caused heart changes, delayed kidney function, and decreased life expectancy (15-17); however, no effect was observed in another study (18). Some studies have also shown that the quality of life of individuals improved after kidney transplantation (19). In this regard, changes in PH intensity have been implicated in the rate of change in quality of life. Due to the fact that the results of different studies in Iran and other countries on the prognostic effect of PH on transplanted kidneys are not completely identical and the racial context of our society is different, the present research aimed to assess the effect of PH before transplantation on mortality, kidney function, and quality of life of patients.

## Materials and Methods

This cohort study was performed on 60 patients with ESRD who underwent kidney transplantation in nephrology clinics in hospitals in Ardabil, Iran, from August 2019-August 2020 and were followed up for one year. The inclusion criteria entailed the age range of over 18 years, preoperative echocardiography, and willingness to be followed up for at least one year. On the other hand, the exclusion criteria were as follows: connective tissue disease other than lupus, HIV infection, congenital disease heart, acute heart failure, port hypertension, interstitial lung disease, sleep apnea, pulmonary artery occlusion by embolism, tumor or foreign body, and severe pre-transplant pulmonary hypertension. Serum urea, creatinine, and GFR levels of patients were measured before transplantation and one year later; moreover, echocardiography was performed before transplantation. In addition, the 12-item health-related quality of life questionnaire (SF-12) was completed for patients before and one year after the transplantation.

The patients were assigned to three groups in terms of etiology: 1- Patients without PH, 2-Patients with mild PH

before transplantation, and 3- Patients with moderate PH before transplantation. The PH intensity was considered mild (25-45 mmHg), moderate (60-45 mmHg), and severe (above 60 mmHg) based on SPPA, and the severe cases were excluded from the study. Patients were evaluated for mortality, hospitalization, and renal failure during one year of follow up. To examine the quality of life of dialysis patients after transplantation, SF-12 was used before transplantation and one year after later. The collected data were analyzed in SPSS software (version 24).

## Results

In this study, 60 ESRD patients undergoing routine hemodialysis who were candidate for kidney transplantation were selected. The mean age of patients was  $40.43 \pm 13.59$  years (the age range of 19-70 years). Out of 60 patients, 37 (61.7%) and 23 (38.3%) cases were male and female, respectively. hypertension, diabetes, lupus, autosomal dominant polycystic kidney disease, and ischemic heart disease were observed in 51.7%, 23.3%, 1.7%, 6.7%, and 6.7% of

patients, respectively. In echocardiographic findings, the mean left ventricular ejection fraction (LVEF) was reported as  $54.08 \pm 6.68\%$ . The lowest and highest LVEF rates were 28% and 61%, respectively. The average pulmonary artery systolic pressure (PASP) was  $36.95 \pm 12.22$  with a mean of 35 mmHg. The lowest and highest PAP levels were 17 and 60 mmHg, respectively. According to PASP findings, PH was present in 50 (83.3%) patients, including 30 (50%) cases of mild PH and 20 (33.3%) cases of moderate PH. According to the results of the SF12 questionnaire, it was demonstrated that quality of life in patients after transplantation significantly increased from  $31.05 \pm 6.77$  to  $36.6 \pm 6.50$  ( $P < 0.001$ ). Moreover, the GFR of these patients increased from  $14.82 \pm 12.26$  to  $70.75 \pm 21.60$  after transplantation ( $P < 0.001$ ). There was no significant difference between patients with and without PH in terms of age and gender, pre and postoperative GFR, and changes in quality of life and GFR following transplantation. Nevertheless, ESRD patients with PH had a lower quality of life than patients without PH (Table 1).

**Table 1:** Compare demographic, clinical, and laboratory findings between patients with and without PH

Variables	With pulmonary hypertension	Without pulmonary hypertension	P-value
Age	$41.7 \pm 13.1$	$34 \pm 14.9$	0.1
Gender	Female	17(34%)	0.27
	Male	33(66%)	
Quality of life before transplantation	$30 \pm 6.2$	$36.1 \pm 7.7$	0.009
Quality of life after transplantation	$36.3 \pm 6.5$	$38.4 \pm 6.9$	0.36
GFR before transplantation	$14.9 \pm 12.8$	$14.3 \pm 10$	0.87
GFR after transplantation	$70 \pm 22.3$	$74.5 \pm 18.2$	0.55
Improving rate in quality of life	$29.1 \pm 7.4$	$7.7 \pm 3.7$	0.2
Improving rate in GFR	$524.4 \pm 314$	$564 \pm 312$	0.71
GFR: glomerular filtration rate			

As displayed in Table 2, which compares demographic, clinical, and laboratory findings between patients based on PH intensity, the mean age of patients increased with an increase in PH intensity.

In addition, the mean age of patients with moderate PH was significantly higher, as compared to that in patients with mild PH ( $P = 0.002$ ) and without PH ( $P = 0.006$ ).

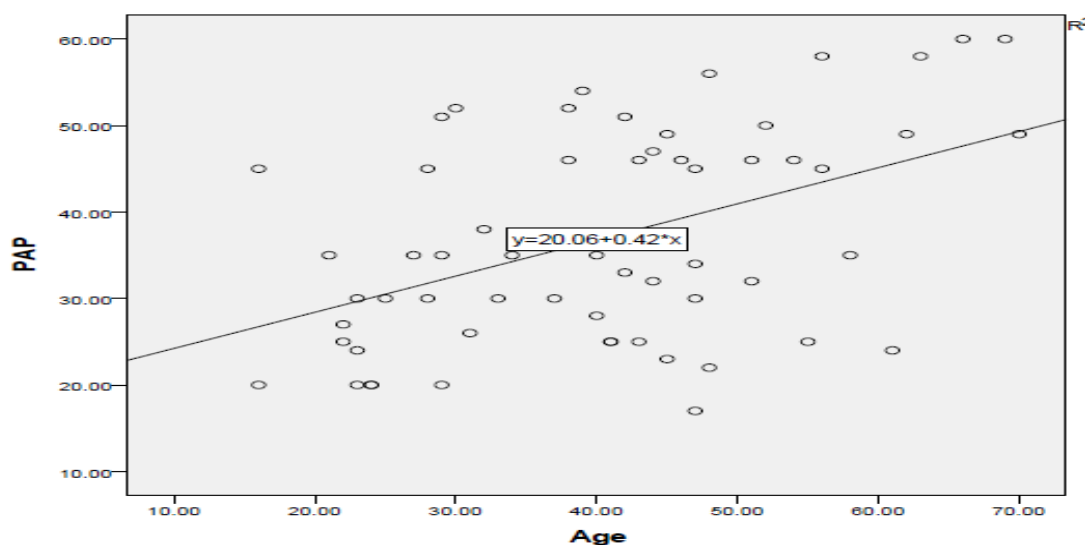
**Table 2:** Compare demographic, clinical, and laboratory findings between patients by PH severity

Variables		Mild pulmonary hypertension	Moderate pulmonary hypertension	Without pulmonary hypertension	P-value
Age		36.7±11.3	49.3±12.2	34±14.9	0.001
Gender	Female	11(37%)	6 (30%)	6 (60%)	0.27
	Male	19 (63.3%)	14 (70%)	4(40%)	
Quality of life before transplantation		30.83±5.5	28.9±7.1	36.1±7.7	0.01
Quality of life after transplantation		34.7±6.6	38.8±5.6	38.4±6.9	0.06
GFR before transplantation		16.1±15	13.3±8.6	14.3±10	0.72
GFR after transplantation		70.63±23.04	69.1±21.7	74.5±18.2	0.81
Improving rate in quality of life		17.4±6.7	46.6±15	7.7±3.7	0.03
Improving rate in GFR		499±309	562.2±326	564±312	0.73

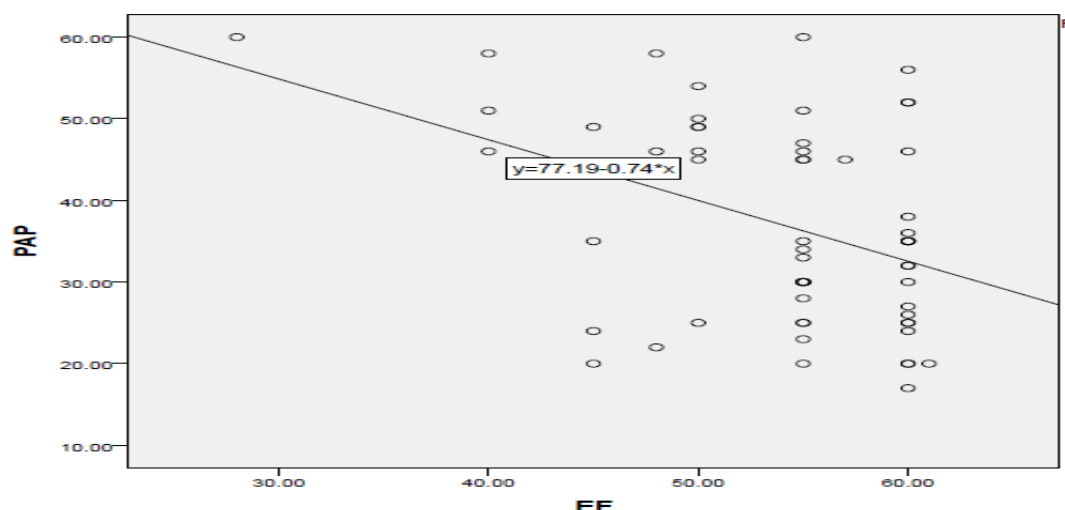
GFR: glomerular filtration rate

Quality of life before transplantation had a statistically significant difference between the two groups. As the PH intensity increases, quality of life decreases. The comparison between the two groups showed that there was only a statistically significant difference between individuals without PH and moderate PH (P=0.01). Furthermore, the rate of improvement in quality of life after transplantation was higher in subjects with moderate PH, as compared to that in other cases; nonetheless, in the comparison between the two groups, no difference was observed in this case and other parameters. There were no cases of death or re-admission to the hospital during one year of follow up for patients, and therefore, they were not included in the

analysis. In another part of the study, the relationships between PH and other variables was assessed using Pearson's Correlation test. The PASP level was positively correlated with age of patients (r=0.465; P<0.001) (Figure 1) and improvement in quality of life after transplantation (r=0.288; P=0.02). Moreover, the results pointed to negative correlation of PASP level with LVEF level (r=-0.407; P=0.001) (Figure 2) and quality of life before transplantation (r= 0.229; P=0.02). However, PASP was not significantly associated with quality of life after transplantation (r=0.2; P= 0.12), GFR before (r=0.068; P= 0.6) and after transplantation (P=0.82; r=0.030), as well as the amount of GFR changes (r= 0.096; P=0.46).



**Figure 1:** Relationship between PASP level and age of patients



**Figure 2:** Relationship between PASP and LVEF level

## Discussion

Despite the numerous benefits of kidney transplantation as a treatment for kidney failure in dialysis patients, it can be associated with psychological and social burden. Multiple laboratory findings improve, while some preclinical findings can worsen. On the other hand, kidney transplantation can enhance the quality of life among dialysis patients and improves their morale. Furthermore, higher quality of life before transplantation is associated with improved survival and reduced mortality (20). As expected, following kidney transplantation during follow up, a significant improvement was achieved in GFR level and function of all patients, as well as the quality of life in these patients. In their study, Von der Lippe et al. found that quality of life parameters improved significantly after transplantation (21). In a similar vein, the results of a study by Kostro et al. pointed to an improvement in quality of life after transplantation, as compared to before this treatment, regardless of the type of treatment received (22). In another recently published study, Iqbal et al., observed that the quality of life significantly improved after kidney transplantation in ESRD patients, compared to that in the pre-kidney transplant period (23). Cannavò et al., in their study on patients, who were on the transplant list for any reason, found that the quality of life in these people was much lower than transplanted people (24). There are

several factors involved in the achievement of a better quality of life. Manifestations and severity of clinical symptoms, available demographic findings, level of social support, and the presence of depression, as well as access to cyberspace, are involved in the quality of life among dialysis patients (25). In confirmation of the aforementioned findings in the present study, patients with preoperative PH significantly had a lower quality of life, in comparison with those without preoperative PH. In a similar way, in the study by Matai et al., it was observed that there was a significant relationship between quality of life and the severity of pulmonary hypertension—that is to say, quality of life determines the consequence of treatment (19). Reis et al., in another study, evaluated the relationship between any type of pulmonary arterial hypertension (PAH) and quality of life and stated that the quality of life in patients with PAH is not desirable and worsens with an increase in the severity of symptoms (26).

Along the same lines, Kivanç et al., compared the quality of life in the three dialysis groups with PH, non-dialysis patients with PH, and healthy patients. They observed a significant difference between the three groups in terms of quality of life subgroups (27). The reason for the lack of communication is that ESRD has so many negative effects on quality of life that the effect of PH alone on quality of life is not visible.

In the present study, there was no difference in GFR level before and after transplantation, improvement in quality of life, and GFR between ESRD patients with and without PH before transplantation. In a similar vein, Goyal et al., stated that although PH is not an independent determinant of delayed kidney function in ESRD patients, those with PH are more prone to postoperative hypertension and delayed kidney function (18).

Contrary to the above findings, in the study by Wang et al., an increase in PASP was associated with a significant decrease in eGFR during one year and two years after transplantation (14). In the study by Foderaro et al., it was observed that the rate of graft failure in patients with PH was three times higher, as compared to that in patients without PH. There was also an increase in creatinine levels after transplantation in people who did not have this disorder (17). Nevertheless, in the present study, the evaluation of the relationship between variables revealed that an increase in pulmonary pressure resulted in a significant decrease in quality of life after transplantation and also a decrease in the rate of improvement in quality of life.

In the general public, left heart disease and chronic hypoxic pulmonary disorders are the most common causes of PH. Previous studies have pointed out that the duration of dialysis, hemodialysis through arteriovenous fistula (AVF), and the amount of LVEF are independent determinants of PH (28). In a study performed by Issa et al., the duration of dialysis has also been reported as an independent factor in the incidence of PH in ESRD patients (15). Low LVEF, ischemic heart disease, heart failure, valvular heart disease, and AVF are other causes responsible for PH progression among ESRD patients (29,30).

In the present study, a significant negative relationship was observed between PH level and LVEF level. Regarding the limitations of the present study, with the prevalence of Covid-19 pandemic, the number of kidney transplants has dramatically decreased in the province and it was not possible to evaluate a large number of patients. In the assessed patients, PH changes after

transplantation were not evaluated, and therefore, the effect of transplantation on possible PH changes was not measured. Lack of regular referral of patients for evaluation was another notable limitations of this study.

According to the findings of the present study, it can be stated that kidney transplantation improves kidney function and quality of life. Moreover, the presence of PH leads to poor quality of life in ESRD patients before kidney transplantation. Furthermore, kidney transplantation improves the quality of life in people with mild or moderate PH before transplantation. Nonetheless, there was no significant difference between PH intensity and quality of life after transplantation, and PH intensity had no effect on the consequence of kidney transplant.

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