ACTA ABP BIOCHIMICA POLONICA

Vol. 68, No 4/2021
717–724
https://doi.org/10.18388/abp.2020_5619

Regular paper

Impact of tobacco smoking on pulmonary and kidney function after successful kidney transplantation – A single-centre pilot study

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The all consequences of tobacco smoking on the lungs and kidney function in kidney transplant recipients are unknown. We investigate the impact of tobacco smoking on lung and kidney functions in kidney transplantation recipients. Methods: Finally, 55 patients were evaluated after kidney transplantation (age 50.8±13.4). Pulmonary function was performed using spirometer Pneumo Screen; anthropometry with body composition using electronic scale, dynamometer, and multi-frequency bioimpedance analysis. Biochemical parameters were measured in serum, eGFR was calculated according to the CKD-EPI formula. Results: Smoking history was reported by 23 kidney transplant recipients (42%); among them 12 (22%) were current smokers (mean pack-years=28.3±15.2). There were significant differences of spirometry parameters (FEV1, FEV1/FVC, MMEF% predictive value) between non-smokers vs active smokers ($p<0.003$; $p<0.005$; $p<0.04$; respectively). Current smokers presented significantly lower eGFR and higher IL-6 serum levels compare to both-past smokers and non-smokers ($p<0.02$; $p<0.04$ respectively), the other biochemical parameters did not differ between these groups. The pack-years positively correlated with MRC dyspnoe scale and triglycerides, and negatively with HDL cholesterol levels. Conclusions: Active tobacco smoking was relatively common in kidney transplant recipients and was associated with poorer pulmonary function, systemic inflammation, and its possible impact on kidney graft. Other parameters of inflammation associated with renal function should be studied in active smokers before and after kidney transplantation. Effective smoking cessation programs are required in patients before and after kidney transplantation.

Key words: tobacco smoking, pulmonary function, kidney function, kidney transplantation

Received: 20 February, 2021; revised: 27 March, 2021; accepted: 21 April, 2021; available on-line: 24 June, 2021

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Acknowledgements of Financial Support: This study was supported by the Medical University of Gdańsk, Poland (ST445 and 02-0549/07)
Abbreviations: BMI, Body Mass Index; CKD, Chronic kidney disease; CRP, C-reactive protein; eGFR, estimated Glomerular Filtration Rate; F, Body Fat; FVC, forced vital capacity; FEV1, forced expiratory volume in 1second; HDL, High density lipoprotein; IL-6, interleukin 6; KTRs, kidney transplant recipients; LDL, Low density lipoprotein; LTI, Lean Tissue Index; MMEF, maximal mid-expiratory flow; MRC, Medical Research Council; PEF, peak expiratory flow; TG, Triglycerides; TBW, Total Body Water

INTRODUCTION

Chronic kidney disease (CKD) may impact other organs function, including the respiratory system, and may require a kidney transplant. Disorders in pulmonary function were demonstrated already in pre-dialysis patients as decreased maximal and submaximal exercise tolerance (Clyne, 2004; Faria *et al.*, 2013; Sandilands *et al.*, 2013; Wallin *et al.*, 2018). Pulmonary complications worsened significantly in dialysis patients. Several abnormalities including interstitial and alveolar oedema, pulmonary hypertension, hemosiderosis, fluid overload and premature airway closure, ventilation-perfusion mismatching and weakness of the pulmonary muscles were reported in these patients (Yigla *et al.*, 2003; Nascimento *et al.*, 2004; Yigla *et al.*, 2009; Kosmadakis *et al.*, 2013). There was also a further deterioration in exercise tolerance and decreased diffusion capacity due to several factors of the dysfunctional kidney (Ferrer *et al.*,1990; Herrero *et al.*, 2002; Hekmat *et al.*, 2007; Sahni *et al.*, 2014). Kidney transplantation is currently the best method that improves the quality of life and prolongs the survival of patients with CKD (Ojo *et al.*, 2000). Improvement of kidney function is associated with more effective removal of uremic toxins, improved nutritional status and increased exercise tolerance in kidney transplant recipients (KTRs) compared to haemodialysis patients (Bush *et al.*, 1991; Violan *et al.*, 2002; Kalender *et al.*, 2002; Karacana *et al.*, 2006; Bozbas *et al.*, 2009; Alhamad *et al.*, 2014; Coelho *et al.*, 2008; Pencheva *et al.*, 2015).

On the other hand, there are factors that impair lung function in patients after kidney transplantation. The KDIGO Transplant Working Group (KDIGO, 2009) points to cigarette smoking in KTRs as an independent risk factor for patient survival, graft survival, ischemic heart disease, cerebral vascular disease and chronic heart failure (Aker *et al.*, 1998; Arend *et al.*, 1997; Kasiske *et al.*, 1996; Lentine *et al.*, 2005; Cosio *et al.*, 1999). Smoking was also found to be associated with posttransplant malignancies (Dantal *et al.*, 2007). Although The European Best Practice Guideline Group (EBPG) recommends that smoking should be stopped before kidney transplantation, some individuals still remain active smokers even after transplantation (Abramowicz *et al.*, 2015).

However, there is little information available regarding pulmonary function parameters in smoking KTRs and the impact of smoking on the functioning of the kidney graft.

The aim of the study was to investigate the smoking habits and the tobacco smoking impact on lung and kidney functions in a group of KTRs.

MATERIAL AND METHODS

Study design

This was a prospective study of Polish KTR (Caucasian race) patients recruited between January 2017 and December 2019, at the Medical University of Gdansk in Poland. The study had received approval from the Bioethics Committee of the Medical University of Gdańsk no. NKBBN/417/2015.

Study Population

The inclusion criteria were as follows: (i) age >18 years old; (ii) successful kidney transplantation at least 1 year before the study; (iii) the ability to undergo pulmonary function tests (PFT); (iiii) stable clinical condition; (iiiii) signed consent. Patients with a diagnosis of a respiratory infection (active or in the last four weeks), thoracic deformity, neurological impairment, uncontrolled hypertension (systolic blood pressure ≥200 mmHg and/or diastolic blood pressure ≥120 mmHg), or using bronchodilators or anticholinergics in the previous two days, were excluded from the study.

Smoking Habits

The smoking history was recorded from patients' interviews based on a series of yes/no questions; then subjects were classified into the following groups: nonsmokers (never smoking), pretransplant smokers (duration at least 5 pack-years, stopped smoking at least 12 months before transplantation) or current smokers. In smokers, smoking duration (years) and the number of cigarettes (packs per day) were defined as pack-years.

Pulmonary Assessment

A complete physical examination was performed and clinical manifestations of the pulmonary system dysfunction such as a persistent cough (longer than 8 weeks), dyspnoea (according to the Medical Research Council - MRC), dyspnoea scale, poor tolerance of exercise (the questionnaire for the poor tolerance of exercise) were recorded. The MRC dyspnoea scale defined the degree of shortness of breath; there were five grades: grade 1, "I only get breathless with strenuous exercise"; grade 2, "I get short of breath when hurrying on the level or up a slight hill"; grade 3, "I walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level"; grade 4, "I stop for breath after walking 100 yards or after a few minutes on the level"; grade 5, "I am too breathless to leave the house" (Bestall *et al.*, 1999).

Pulmonary Function Tests

Spirometry was performed in all subjects using the calibrated, computerized spirometer (PneumoScreen, Jaeger, Germany), according to the European Respiratory Society (ERS) and American Thoracic Society (ATS) recommendations (Miller *et al.*, 2005) by certificated spirometry technicians. The reversibility test with a bronchodilator (400 μg salbutamol) was also performed and spirometric values before and 20 minutes after the administration of a short-acting bronchodilator were recorded. Forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), peak expiratory flow (PEF), maximal mid-expiratory flow (MMEF), and FEV1/FVC expressed as litres (L), and a percentage of predicted normal values (%pv) were evaluated. Abnormal lung function was defined as obstruction if FEV1 was <80%pv and FEV1/FVC ratio reduced <0.7, and restrictive disorder if FVC was <80%pv and FEV1/FVC ratio≥0.7 as recommended according to the ATS/ERS guidelines.

Anthropometry

Anthropometry and body composition were assessed using: electronic scale, dynamometer and multi-frequency bioimpedance analysis. BMI – body mass index – was estimated according to the current body mass/height^2 (kg/m^2). BMI value below 18.5 was considered underweight, 18.5–24.99 – normal range; 25–30 as overweight, above 30 as obesity. Body composition was evaluated by BIA – Multifrequency Bioimpedance Analysis method (using BCM – Body Composition Monitor, Fresenius S.A., Germany).

Kidney Laboratory Parameters

Blood samples were taken after 12 hours of overnight fasting and the following tests were performed on the serum: albumin (s-albumin) level, creatinine level, BUN, lipidogram and morphology by routine methods using Hitachi 911 (Boehringer, Mannheim GmbH); CRP and IL-6 levels by the ELISA method (DRG Instruments GmbH, Germany). eGFR was calculated according to the CKD-EPI formula.

Statistical Analysis

Statistical analysis was performed using Statistica 13.0 version for Windows (StatSoft, Poland). All data were expressed as means ± S.D. Comparisons between groups were examined by the Student's test and U Mann-Whitney test; for comparisons of the variables the Wilcoxon test was used. The Pearson correlation test was used to determine the relationship between continuous variables and the Spearman correlation test was used for nonparametric variables**.** Independent associations between the variables were assessed with stepwise multiple regression analysis. The p-value <0.05 was considered statistically significant for all analyses.

RESULTS

Study Population

Finally, 55 out of 72 KTRs met the inclusion criteria (35/20 male/female with mean age 50.7±13.7 years). All patients were in a clinically stable condition and were treated with triple immunosuppressive IS protocols including calcineurin inhibitor (cyclosporine or tacrolimus), mycophenolate mofetil, and steroids. The basic characteristics of the study population are presented in Table 1.

Smoking Habits and Pulmonary Function Assessment

Smoking history was reported by 23 KTRs (42%), among them about half (12) were current smokers. The patients smoked a mean of 0.9 pack/per day (pack-years = 28.3±15.2). The clinical symptoms of pulmonary dysfunction recognised in the study group are shown in Table 2.

Table 1. The basic characteristics of the study patients (n=55)

Parameters	Kidney Transplant Recipients	Normal range
Age (years)	50.7±13.7	–
M/F	35/20	–
Transplantation vintage in months	100.1±68.1 (range 19-349)	–
eGFR (ml/min/1.73 m²) acc. CKD-EPI	53.4±22.3 (range 22.1-100.1)	>60
Creatinine (mg/dl)	1.43±0.46 (range 0.69-3.22)	0.55-1.02
BMI (kg/m²)	26.2±4.5 (range 19.9-39.0)	18.5-24.99
Albumin (g/l)	37.1±4.8	35-50
CRP (mg/l)	3.1±2.7	0.1-5.0
IL-6 (pg/ml)	1.6±0.5	1.4-14.1
Haemoglobin (g/dl)	13.1±1.8	11.5-16.0
Total Cholesterol (mg/dl)	198.5±45.8	138-200
HDL (mg/dl)	55.2±18.1	M 35-70; F 40-80
LDL (mg/dl)	110.9±43.5	<135
TG (mg/dl)	159.3±68.3	<150

Abbreviations: eGFR, estimated Glomerular Filtration Rate; CKD-EPI, Chronic Kidney Disease - epidemiology formula**;** BMI, Body Mass Index; CRP, C-reactive Protein; IL-6, Interleukin 6; LDL, Low-Density Lipoprotein; HDL, High-Density Lipoprotein; TG, Triglycerides

Table 2. Clinical symptoms of pulmonary dysfunction in smokers and non-smokers

	All n=55	Non-Smokers	Smokers		Non-smokers vs Current smokers
		n=32	Past n=11	Current n=12	
Intolerance of exercise	12 (22%)	4 (12.5%)	1 (2%)	7 (58%)	Ch^2=38.6, Df=24, p=0.02
Persistent cough	8 (14.5%)	3 (9%)	0	5 (41.6%)	Ch^2=9.3, Df=2, p=0.009
Dyspnoea	10 (18%)	3 (9%)	0	7 (58%)	Ch^2=20.6, Df=8, p=0.008

Data expressed as the number of patients (%)

The most common symptoms reported by patients were reduced exercise tolerance (22% of patients) and dyspnoea (18% of patients), however, the results of the MRC scale assessment showed that 30% of KTRs displayed different levels of dyspnoea (Fig. 1).

PFT results are shown in Table 3. There were significant differences in FEV1, FEV1/FVC, PEF, and MMEF values between non-smokers vs active smokers (p<0.003, p<0.005, p<0.04, and p<0.01, respectively). However, there were no differences between non-smokers vs past-smokers (FEV1 p<0.06; FEV1/FVC p<0.55; PEF p<0.32; MMEF p<0.06).

Over 70% of patients presented normal values of PFT results (n=40). A decreased pulmonary function in spirometry was found in 15 KTRs, of which 7 were current smokers, 4 past smokers, and the remaining – never smoked. Obstructive disorders were observed in 11 and restrictive disorders in 4 KTRs (Fig. 2). A positive reversibility test result was found in 4 of KTRs. The current smokers more frequently presented bronchial obturation and clinical symptoms: low tolerance of physical

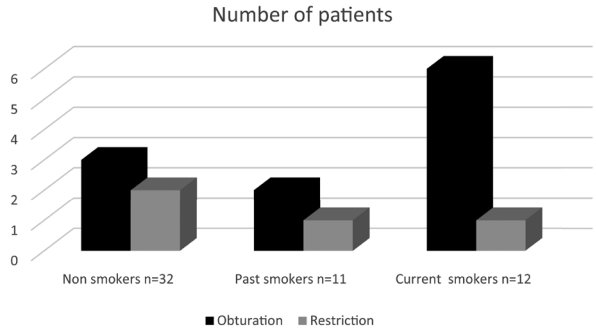

Figure 1. Dyspnoea according to MRC scale (% of patients). Description of MRC scale grades is in the text.

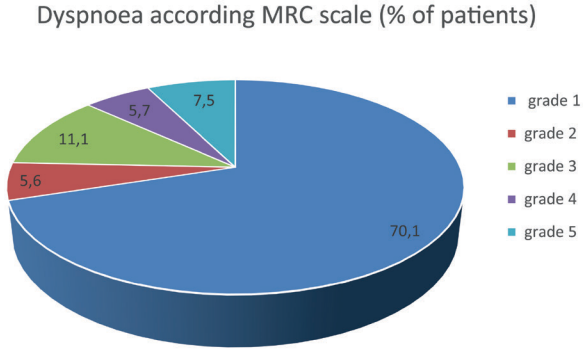

Figure 2. The number of patients with obturation or restriction in the non-smokers, past smokers and current smokers groups.

Table 3. Results of the pulmonary assessment in smokers and non-smokers

	All n=55	Non-smokers	Smokers		*p*-value*,**
		n=32	Past n=11	Current n=12	
FEV1	91.3±19.9	95.0±16.6	96.0±18.6	77.5±16.6	0.003 0.06
ΔFEV1	4.7±5.7	4.0±5.6	4.0±6.0	7.0±6.0	0.26 0.27
FVC	99.1± 16.8	102±15.7	98.0±14.6	91.3±20.1	0.058 0.36
FEV1/FVC	93.7±12.1	95.0±10.4	99.0±7.3	85.5±4.5	0.005 0.55
PEF	81.6±16.9	85.0±14.2	81.0±20.5	73.2±18.6	0.04 0.32
MMEF 75-25	64.8±31.2	71.0±29.3	71.0±28.8	45.0±32.0	0.01 0.06

Data expressed as percent of predicted values, mean ±S.D.; FEV1, Forced Expiratory Volume in 1 Second; FVC, Forced Vital Capacity; PEF, Peak Expiratory Flow; MMEF, Maximal Mid-Expiratory Flow. **p*-value=non-smokers *vs* current smokers/***p*-value=non-smokers *vs* past smokers

activity, dyspnoea and a persistent cough, compared to past smokers and non-smokers (Table 2).

Anthropometric and Biochemical Parameters

There were no differences in body mass, BMI, and body composition between smokers and non-smokers, and also between pretransplant and current smokers (Table 4). Current smokers presented significantly lower eGFR and higher IL-6 serum levels in comparison to both – past smokers and non-smokers ($p<0.02$ and $p<0.04$, respectively), while the other biochemical parameters did not differ significantly between these groups. The anthropometric and biochemical results in smokers and non-smokers are presented in Table 4.

Correlation Between Smoking, Pulmonary Function, and Biochemical Parameters

The pack years positively correlated with the MRC scale (R Spearman=0.45, $p<0.05$) and TG levels (R Spearman=0.40, $p<0.05$) and negatively with HDL cholesterol levels (R Spearman =–0.62, $p<0.05$).

DISCUSSION

The study provided insight on the cigarette smoking habits and pulmonary outcomes measured by spirometry in adult patients at least 1 year after successful kidney transplantation. All of the studied individuals were previously treated with haemodialysis due to CKD, then received a kidney from a deceased donor followed by triple immunosuppression.

The most important finding of this study is that after a kidney transplant, over 20% of patients still smoked cigarettes. Active smokers presented lower eGFR and higher IL-6 levels and more often an obstructive pattern in pulmonary function tests with reduced physical activity tolerance and dyspnoea, compared to non-smoking KTRs.

There are some publications on tobacco smoking in KTRs (Yavuz *et al.*, 2004; Kheradmand *et al.*, 2005; Banas *et al.*, 2008). In contrast to our population, the PRETAGREF study (Béchade *et al.*, 2016) showed that the prevalence of smoking is not high in transplanted patients in France, where only 6% of KTRs reported current tobacco use. The authors suggested that environmental factors are associated with failure in tobacco cessation. Among them, living alone and exposure to second-hand smoke are associated with smoking. In the FAVORIT trial (Weinrauch *et al.*, 2018), 11% of KTRs from Brazil, Canada and the USA were currently smoking, 39% were former smokers, 50% never smoked. Up to 25% of patients who continued smoking after transplantation among 402 KTRs were reported in a Hungarian study (Gombos *et al.*, 2010). This result is similar to our Polish population study in which smoking history was reported by 42% KTRs and among them, 22% were current smokers. In spite of the fact that smoking cessation is recommended for future transplant recipients and renal transplantation is a strong incentive for patients to stop smoking (Banas *et al.*, 2009), some of KTRs do not follow the recommendations (Anis *et al.*, 2019).

Another interesting finding in our study was the lower eGFR in active smokers compared to non-smokers. Since these groups did not differ in demographic and clinical factors, it can be concluded that one of the factors affecting the deterioration of the functioning of the transplanted kidney is current smoking. Moreover, it is important that the lower eGFR was found only in active smokers, and no such effect was observed in patients who quit smoking at least one year before a kidney transplant. Similarly, lower GFR in active smokers was found by other authors (Kasiske *et al.*, 2000; Sung *et al.*, 2001; Gombos *et al.*, 2010). In contrast to these findings, no association was found by Mohamed *et al.* while Nogueira *et al.* showed that smoking is not a modifiable risk, describing worse outcomes in KTRs who were active smokers and quit smoking at least 5 years before transplant compared with those who never smoked (Mohamed *et al.*, 2009; Nogueira *et al.*, 2010).

It is known that many factors contribute to diminished long-term transplant outcomes, including chronic allograft nephropathy, recurrence of the primary disease, hypertension, and viral infections (Spasovski *et al.*, 2005; Gratziou, 2009). Besides these, smoking also may cause many adverse consequences in transplant recipients. Smoking by KTRs significantly increases the risk of cardiovascular events, renal fibrosis, transplant rejection, and malignancy (Corbett *et al.*, 2012). Ponticelli *et al.* showed that the development of de novo cardiovascular insult in the first year post-transplant, in addition to

Table 4. Anthropometrical and biochemical parameters in smokers and non-smokers

	All n=55	Non-Smokers	Smokers		*p*-value*,**
		n=32	Past n=11	Current n=12	
Age (years)	50.7±13.7	47±14.4	56±8.0	56.1±13.3	0.13 0.06
M/F	28/27	16/16	12/11	7/5	-
Transplantation vintage in months	100.1±68.1	70±59.1	91±105.4	69.8±50.9	0.81 0.43
Kidney Laboratory Parameters					
eGFR (ml/min/1.73 m²) acc. CKD-EPI	53.4±22.3	58±21.4	60± 27.9	39.6± 13.6	0.02 0.85
Creatinine (mg/dl)	1.43±0.46	10.1±0.4	2.0 ±0.4	1.6± 0.6	0.40 0.28
BMI (kg/m²)	26.2±4.5	26±4.5	26±4.9	26.1±4.7	0.95 0.87
Albumin (g/l)	37.1±4.8	38.1±4.5	35±3.0	36.6±7.1	0.77 0.29
CRP (mg/l)	3.1±2.7	3.0±1.9	4.0±4.5	3.3±1.7	0.84 0.21
IL-6 (pg/ml)	1.6±0.5	1.4±4.1	1.1 ±2.6	2.5±1.0	0.04 0.05
Haemoglobin (g/dl)	13.1±1.8	13.9±1.9	14±1.8	13.7±1.4	0.44 0.61
Cholesterol (mg/dl)	198.5±45.8	204.0±48.4	195.0±36.5	187.9±50.3	0.42 0.58
HDL (mg/dl)	55.2±18.1	62±14.9	48±12.4	45.4±22.5	0.18 0.05
LDL (mg/dl)	110.9±43.5	118±56.9	110±28.5	97.4±27.5	0.44 0.74
TG (mg/dl)	159.3±68.3	131±63.2	216±64	162.8±47.1	0.87 0.60
Body composition					
F(%)	32.8±9.0	32.0±7.1	30.1±12.2	36.0±15.6	0.05 0.21
F (kg)	24.9±9.9	24.0 ± 0.3	23.0± 0.6	29.0±14.2	0.16 0.32
LTI (kg/m²)	13.1±2.2	13.0 ±4.9	13.0±10.6	12.0±1.8	0.21 0.89
TBW (%)	49.6±7.0	50.0 ±6.2	48.6±6.9	46.0±7.7	0.09 0.74
TBW (kg)	36.5±7.1	37.0±7.7	38.0±7.8	35.0±4.8	0.51 0.52

Data is presented as mean ±S.D.; **p*-value=non-smokers *vs* current smokers/***p*-value=non-smokers *vs* past smokers; KTRs, kidney transplant recipients. **Abbreviations**: eGFR, estimated Glomerular Filtration Rate; CKD-EPI, Chronic Kidney Disease, epidemiology formula; BMI, Body Mass Index; CRP, C-reactive Protein; IL-6, Interleukin 6; LDL, Low-Density Lipoprotein; HDL, High-Density Lipoprotein; TG, Triglycerides; F, Body Fat; LTI, Lean Tissue Index; TBW, Total Body Water

other factors such as pre-existing cardiovascular disease, older age, pre-transplant hypertension, duration of dialysis, was associated with smoking (Ponticelli *et al.*, 2002). Other studies suggested potentially harmful effects of the degree of exposure to smoking on the progression of CKD (Cosio *et al.*, 1999; Zitt *et al.*, 2007; Nguyen *et al.* 2007; Orth *et al.*, 2008; Weinrauch *et al.*, 2018). The relationship between smoking and the duration of the transplant was also highlighted by Aref *et al.* (Aref *et al.*, 2017). The explanation for this association was not clearly defined. One possible explanation of this phenomenon is increased fibrous intimal thickening of small arteries in the renal transplant in smokers (Cosio *et al.*, 1999). Other investigators (Kasiske *et al.*, 2000) suggested less adherence to the medications in smoking patients or endothelial dysfunction caused by vascular production of reactive oxygen species (Raij *et al.*, 2001) as well as transient increases in blood pressure accompanied by a decrease in both glomerular filtration rate and effective renal plasma flow (Halimi *et al.*, 1998).

We would like to provide one more explanation for the adverse effects of smoking on the function of kidney graft. In the present study, we found that 36% of KTRs presented abnormalities in pulmonary function; mainly obstructive patterns and also increased concentration of IL-6 in the plasma.

Some studies showed that CKD can cause deterioration of lung function and, moreover, this effect is sup-

ported by the fact that pulmonary function can improve after transplantation, regardless of the type of changes found in the respiratory system (Guleria *et al*., 2005).

The other authors studied pulmonary function in 49 dialysis patients and 24 KTRs and showed that there was airway obstruction in small-airway in dialysis patients, which subsided after kidney transplantation. KTRs also showed higher exercise tolerance than haemodialysis patients (Karacana *et al*., 2006). In another study, Guleria *et al.* found that the clinical symptoms: dyspnoea, hypoxia, the restrictive pattern of pulmonary function, and respiratory muscle weakness in 29 haemodialysis patients improved after kidney transplantation (Guleria *et al*., 2005). Unfortunately, we could not compare pulmonary function before and after renal transplantation, because it was possible to perform spirometry in our subjects only after the transplantation. But interestingly, in our study, the obstructive pattern of bronchi with negative reversibility test was presented mainly by active smokers. They also reported clinical symptoms such as reduced tolerance to exercise and dyspnoea.

It is well known that tobacco smoking is a risk factor for pulmonary diseases like chronic obstructive pulmonary disease (COPD), asthma, or lung cancer in the healthy population (Mannino *et al*., 2007). Also, COPD is reported in patients with CKD and KTRs; for example, the prevalence of COPD was 7.5% in the cohort of CKD in the United States (Collins *et al*., 2011). It was proven that moderate and severe COPD are related to increased long-term mortality in patients with CKD (Gan *et al*., 2004; Kent *et al*., 2012; Weis *et al*., 2015). Besides the fact that COPD is considered lung disease, it causes systemic consequences. One of them is chronic systemic inflammation that can have important pathophysiological and therapeutic implications for many organs (muscle strength weakness, eating disorders, cardiovascular disease, osteoporosis, obstructive sleep apnea). Some studies showed that an increased intensity of systemic inflammation is associated also with reduced lung function (Yvette *et al*., 2009). Because IL-6 is an important pro-inflammatory cytokine and has been implicated to play a role in the systemic inflammation in patients with COPD we assessed the IL-6 serum level in KTRs, and it was higher in those currently smoking compared to past-smokers and non-smokers.

Our result that an obstructive pattern and higher serum IL-6 concentrations were presented by smoking KTRs compared to non-smoking subjects was supported by Weis *et al.* (Weis *et al*., 2015). Therefore, we conclude that smoking also may have a role in decreasing transplant longevity, by the fact that COPD may indicate an inflammatory process first in the lung and subsequently a systemic chronic inflammation which finally may affects also the kidney transplant. This was another interesting finding in our study and confirmed that the serum level of IL-6 seems to be a sensitive marker of systemic inflammation in smokers that could reduce lung and kidney graft function. What's more, other researchers indicated that COPD in the KTRs population is diagnosed late because of uncharacteristic symptoms (Yvette *et al*., 2009). Several factors such as overhydration, heart insufficiency, and steroids use can make lung disease diagnosis difficult.

It is interesting that in our population the majority of smokers, despite the education of the necessity to quit smoking especially before the transplant procedure, did not stop smoking. Transplant centers implement different policies regarding smoking recipients and allografts from smoking donors (Anis *et al*., 2019). Results of our study indicate the urgent need for the implementation of a tobacco cessation program for patients waiting for kidney transplantation in Poland.

The study limitations included the retrospective nature of the analysis and the relatively small group of patients. However, the results of the present study carry a significant message that persistent cigarette smoking is associated with lung function impairment in KTRs, which indicates the need for lung assessment, and with the lowering of transplanted kidney function and persistent inflammation.

CONCLUSIONS

Tobacco smoking was relatively common in KTRs and was associated with poorer pulmonary function and systemic inflammation with its possible impact on kidney graft. Negative effects of smoking on kidney graft and pulmonary function were observed only in active smokers. Other parameters of inflammation associated with renal function should be studied in active smokers before and after kidney transplantation. Smoking cessation should be a very important part of the management of patients before and after transplantation.

Clinical Implications

It is necessary to pay attention to education about smoking cessation not only during preparation for transplantation but also during the long-term care after kidney transplantation. The main clinical utility of smoking cessation is not only the reduction of a cardio-vascular or cancer risk but also the prevention of the development of lung dysfunction and its possible negative effect on kidney graft functioning.

Statement of Ethics

The study protocol was approved by the Medicine Ethics Committee of Medical University in Gdansk, Poland and was in adherence with the Declaration of Helsinki. All participating patients provided written informed consent.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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