Psychiatria Danubina, 2021; Vol. 33, Suppl. 9, pp 137-139
Medicina Academica Mostariensia, 2021; Vol. 9, No. 1, pp 137-139

WEIGHT GAIN IN LUNG TRANSPLANTATION PATIENTS DURING THE COVID-19 PANDEMIC IN CROATIA

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received: 25.6.2021; revised: 4.8.2021; accepted: 12.8.2021

SUMMARY

Background: *To determine the effect of lockdown measures on lung transplant patients during the COVID-19 pandemic.*

Subjects and methods: *We collected data from Croatian lung transplant patients before and after the lockdown and analyzed changes in weight, BMI, lung function and blood lipid status.*

Results: *An average increase of 3.74 kg (+4.92%) body weight during the 4 month lockdown period was observed. Lung function values and blood lipid status remained stable.*

Conclusion: *Such weight gain could have detrimental effects on the morbidity and mortality of lung transplant patients. Further follow up is needed to determine the long term impacts of this observation.*

Key words: *lung transplantation – COVID-19 - obesity*

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INTRODUCTION

SARS CoV 2, a novel coronavirus, emerged from Wuhan, China in December 2019, spreading around the globe and causing a worldwide pandemic with more than 75 million cases and 1.7 million deaths globally as of December 2020. Governments around the world issued lockdown measures and reallocated health care facilities and resources to fight the pandemic, sacrificing elective procedures and health care visits. Croatia implemented these measures early in the course of the pandemic with success- only 2247 cases and 103 deaths due to COVID-19 were noted with full reopening after 2 months of lockdown on May 5th 2020. While COVID-19 mortality and morbidity at that time remained low, consequences of the paralyzed public health care system are slowly emerging.

Lung transplant (LuTx) recipients require frequent outpatient clinic visits to asses lung function, immune-supressant regimen compliance and other potential complications. Physical activity and regular exercise are important for maintaning health and an adequate functional status after lung transplantation. Respiratoy infections are one of the leading causes of death in LuTx recipients due to the high level of immune-supression, decreased local pulmonary defenses and direct communication of the graft with the enviroment, making an infection with SARS CoV 2 potentially more deadly than in the general population (Raghu & Carbone 2018). These patients are generally aware of these issues and they tended to adhere to protective and lockdown measures rigorously, remaining homebound for most of the pandemic. Although regular follow up was continued by telemedicine during lockdown, the negative effects of the pandemic became apparent after restarting our lung transplant outpatient clinic. In this observational study we aimed to determine the effect of lockdown measures on lung transplant patients during the COVID-19 pandemic.

SUBJECTS AND METHODS

This observational study included all lung transplant patients in Croatia in post-transplant follow-up. We obtained data from medical records and outpatient follow-up visits before and after the lockdown from February until June 2020 and analyzed changes in weight, BMI, lung function tests (FVC, FEV1, FEF50, DLCO) and blood lipid status (total, HDL and LDL cholesterol, triglycerids). Microsoft Excel (Microsoft, Redmond, WA, USA) was used to tabulate data, calculate frequencies, percentages and median ages. The paired t-tests were calculated using IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA).

RESULTS

The total number of patients in follow-up was 45, although complete medical data was available for 43 (95.56%) patients. 21 patients (46.67%) were male, and

Table 1. Lung function and blod lipid values in February and June 2020

	February 2020	June 2020
FVC (avg.)	101% (3.68L)	98.7% (3.68L)
FEV1 (avg.)	89.5% (2.69L)	87.8%(2.68L)
FEF50 (avg.)	81.1% (3.48L)	74.2%(3.24L)
DLCO (avg.)	67.89%	76.37%
Total cholesterol (mmol/L)	4.81	5.16
Triglycerids (mmol/L)	1.74	1.84
HDL cholesterol (mmol/L)	1.67	1.65
LDL cholesterol (mmol/L)	2.36	2.70

FVC = forced vital capacity; FEV1 = forced expiratory volume in 1 second; FEF50 = forced expiratory flow 50%; DLCO = diffusing capacity; HDL = high-density lipoprotein; LDL = low-density lipoprotein

24 (53.33%) female, with a median age of 57 (range 22-69). Lung transplantation was performed for end-stage COPD in 12 (26.7%), pulmonary arterial hypertension (PAH) in 9 (20.0%), cystic fibrosis (CF) in 8 (17.8%), idiopathic pulmonary fibrosis (IPF) in 7 (15.6%) and alpha 1 antitrypsin deficiency (A1ATD) in 6 (13.3%) patients.

Lung function values and blood lipid status remainned stable as shown in table 1. We observed a marked increase in body weight during the lockdown period. The average weight gain was 3.74 kg (95% CI ([3.04, 4.45]), ($t(42) = 10.723$, $p<0.001$), an increase of +4.92% body weight in 4 months. On average BMI values in June were 1.3 higher than BMI values in February (95% CI [1.06, 1.54], $t(42) = 10.906$, $p<0.001$), with an increase from 26.6 to 27.9 kg/m^2. This observation was more pronounced in male patients who gained an average 4.45 kg (1.44 kg/m^2 increase in average BMI) than in female patients who gained 3.13 kg (1.18 kg/m^2 increase in average BMI).

DISCUSSION

While the impact of overweight and obesity on the mortality and primary graft dysfunction (PGD) in the pre transplant and early post transplant period is well known (Upala et al. 2015, Lederer et al. 2011), there is far less data on the association between long term post transplant weight change and outcomes. A large retrospective cohort study (Singer et al. 2003) found that higher weight gain in the first year after lung transplantation was associated with better survival (HR 0.61, 95% CI 0.41 to 0.90) with no association between acute rejection and weight gain. The patients had an increase in BMI of 2.3kg/m^2, corresponding to a weight gain of +10% with many patients becoming overweight or obese after transplantation.

A more recent single center longitudinal retrospective study from Canada documented weight changes up to 15 years post transplant and their association with mortality (Jomphe et al. 2019). Patients with weight gain >10% of transplant weight at 5 years had a 64% decrease in mortality risk compared to patients with stable weight. Weight loss of >10% at 2 years post transplant increased the risk of mortality 2.4-fold. However, the survival benefit of weight gain was only clear in patients with a BMI <25 kg/m2, while patients with a BMI >25 kg/m^2 had a long term survival advantage with decreasing weight trends.

Since most of our patients fall into this category with an average BMI of 26.6 kg/m^2 (before lockdown) we hypothesize that the observed weight gain in our cohort will have a negative effect on outcomes. Singer et al concluded that it is unlikely for lung transplantation patients to develop obesity related complications because of the relatively short median survival of only 4 years in that time period (Singer et al. 2003). The median survival of our patients is 6.9 years, thus development of complications such as new onset diabetes after transplantation (NODAT), hypertension, coronary artery disease, cerebrovascular disease and cholelithiasis is far more likely. The average weight gain trend of 3.74 kg/4 months, if continued, would correspond to a weight gain of 11.2 kg/12 months which is even higher than the first year weight gain in the most obese patients from the Canadian cohort (8.4±10.6 kg) (Jomphe et al. 2019).

CONCLUSION

We plan further prospective follow up of this unique group of patients to determine the long term impacts of this observation on mortality and morbidity of lung transplant patients in Croatia. Although strict individualized weight management was implemented immediately, the worsening of the SARS CoV2 pandemic in the fall and winter of 2020, with another strict lockdown, will present new challenges and complicate the management of these patients.

Acknowledgements: None.

Conflict of interest: None to declare.

Contribution of individual authors:

Feđa Džubur, Latinka Basara, Goran Glodić, Marko Jakopović & Miroslav Samaržija made substantial contributions to the conception and the desing of the work.

Tomislav Šklebar, Ana Hećimović, Mateja Janković, Jelena Knežević, Andrea Vukić Dugac and Gordana Pavliša made substantial contribution to the acquistion, analysis and interpretation of data for the work.

All authors equaly contributed to drafting the work and revising it critically for important intellectual content.

All authors gave final approval of the version to be published

All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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