Clinical Kidney Journal

ckj

OXFORD

era edta
LEADING EUROPEAN NEPHROLOGY

Clinical Kidney Journal, 2021, vol. 14, no. 5, 1483–1484

doi: 10.1093/ckj/sfaa207
Advance Access Publication Date: 5 December 2020
Letter to the Editor

LETTER TO THE EDITOR

Kidney transplantation improving cardiopulmonary exercise responses: still some way to go before conclusive evidence

Afroditi Boutou[1], Danai Faitatzidou[2], Eva Pella[2] and Pantelis Sarafidis [2]

[1]Department of Respiratory Medicine, Papanikolaou General Hospital, Thessaloniki, Greece and [2]Department of Nephrology, Hippokration Hospital, Aristotle University of Thessaloniki, Greece

Comment to: Lim K, Ting SM, Hamborg T *et al.* Cardiovascular functional reserve before and after kidney transplant. *JAMA Cardiol.* 2020; 5, doi: 10.1001/jamacardio.2019.5738
Correspondence to: Pantelis A. Sarafidis; E-mail: psarafidis11@yahoo.gr

In an important recent study, Lim *et al.* [1] first used cardiopulmonary exercise testing (CPET) to assess cardiovascular responses in 81 chronic kidney disease (CKD) Stage 5 patients before and after kidney transplantation, 81 CKD Stage 5 patients who remained wait-listed and 87 hypertensive patients, who served as controls. At baseline, mean maximum oxygen consumption (VO_2max) was significantly lower in the two CKD groups than in controls (20.7 ± 5.8, 18.9 ± 4.7 and 24.9 ± 7.1 mL/min/kg, respectively). During 1-year follow-up, VO_2max significantly increased in transplanted patients to 22.5 ± 6.3 and decreased in wait-listed patients to 17.7 ± 4.1 mL/min/kg, without changing in controls. The authors concluded that kidney transplantation improves cardiovascular functional reserve after 1 year.

Although the study findings are novel, there are several issues that may limit its conclusions. The authors report a 'prospective, nonrandomized, 3-arm, controlled, cohort study', but they use no matching process to have balanced groups, resulting in major baseline differences in parameters affecting cardiovascular profile. The 7-year age difference and 7-month dialysis vintage difference between the kidney transplant and haemodialysis groups make them rather non-comparable. The hypertensive group has a 10-year age difference from transplanted patients, together with 0% prevalence of diabetes and cardiovascular disease, and much higher average blood pressure than both CKD Stage 5 groups, findings incompatible with a randomly selected group.

Most importantly, the choice of hypertensives as controls is, in principal, not justified, due to major differences in the prevalence of traditional and CKD-specific risk factors between CKD Stage 5 and the average hypertensive. Differences in phosphorus, parathormone, albumin, haemoglobin and high sensitivity C-reactive protein levels are large; all these are independently associated with increased cardiovascular risk [2]. Assessing this issue with statistical adjustment for 10 variables in 80-subject groups is not adequate. The study could be more valid with a blinded matching for age, sex and dialysis vintage for CKD Stage 5 groups, as other studies in end-stage renal disease [3], and a similar process to add a more appropriate control group (i.e. CKD Stage 3b–4 patients).

Furthermore, a major effect of haemoglobin changes specifically on CPET parameters is highly likely; a haemoglobin difference of 3 g/dL results in 19% reduction in blood oxygen-carrying capacity and relevant peak VO_2 decrease at any given cardiac output [4]. In low arterial O_2, there is a rapid decrease of O_2 diffusion gradient from blood to mitochondria, resulting in early anaerobic metabolism and low oxygen uptake at anaerobic threshold (VO_2AT). In transplant patients, haemoglobin change was not correlated with VO_2max improvement, but the relevant P-value was 0.05 and haemoglobin levels at study end are not reported. Several limitations exist also regarding CPET analysis [5]. Normal expected VO_2max and VO_2AT values are derived from equations using gender, age, weight and height; thus, using the %predicted values for between-group

Received: 17.9.2020; Editorial decision: 18.9.2020

comparisons is more appropriate, especially with such baseline differences. Of the total CKD patients, 38% received β-blockers, so heart-rate responses during exercise cannot accurately reflect cardiovascular responses. Reporting baseline spirometry is necessary for between-group or within-group comparisons since 50% of subjects were smokers. Finally, as the maximum CPET is an incremental test with a specific duration, the endurance time is an inaccurate index of exercise capacity. Overall, these findings are promising, but they need confirmation by future larger and optimally designed studies.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

This letter to the editor contains no original data.

REFERENCES

1. Lim K, Ting SMS, Hamborg T *et al.* Cardiovascular functional reserve before and after kidney transplant. *JAMA Cardiol* 2020; 5: 420
2. Valdivielso JM, Rodríguez-Puyol D, Pascual J *et al.* Atherosclerosis in chronic kidney disease: more, less, or just different? *Arterioscler Thromb Vasc Biol* 2019; 39: 1938–1966
3. Alexandrou ME, Loutradis C, Schoina M *et al.* Ambulatory blood pressure profile and blood pressure variability in peritoneal dialysis compared with hemodialysis and chronic kidney disease patients. *Hypertens Res* 2020; 43: 903–913
4. Boutou AK, Stanopoulos I, Pitsiou GG *et al.* Anemia of chronic disease in chronic obstructive pulmonary disease: a case-control study of cardiopulmonary exercise responses. *Respiration* 2011; 82: 237–245
5. American Thoracic Society/American College of Chest Physicians. ATS/ACCP statement on cardiopulmonary exercise testing. *Am J Respir Crit Care Med* 2003; 167: 211–277

Clinical Kidney Journal
ckj