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Research article

Effects of prior air pollution exposure on functional recovery after a myocardial infarction

Jordi Bañeras [a,b,c,*], Alejandro Berenguel-Senén [d], Eulogio Pleguezuelos [e], José Antonio Alarcón [f], Jesús Vallejo [g], Paz Sanz-Ayán [h], Juan Izquierdo-García [h], José Garcia [i], Rafael Colman [j], Juan Ignacio Castillo-Martín [h], Eduard Ródenas-Alesina [a,b,c]

[a] *Department of Cardiology, Hospital Universitari Vall d'Hebron, Barcelona, Spain*
[b] *Vall d'Hebron Research Institute, Vall d'Hebron Hospital, Autonomous University of Barcelona, Barcelona, Spain*
[c] *CIBER CV, ISC-III, Madrid, Spain*
[d] *Unidad de Cardiología Preventiva, Servicio de Cardiología, Hospital Universitario de Toledo, Toledo, Spain*
[e] *Servicio Medicina Física y Rehabilitación, Hospital de Mataró, Consorci Sanitari del Maresme, Barcelona, Spain*
[f] *Servicio de Cardiología, Unidad Rehabilitación Cardíaca, Hospital Universitario Donostia/OSI Donostialdea, Donostia, Spain*
[g] *Servicio de Cardiología, Hospital Virgen del Rocío de Sevilla, Sevilla, Spain*
[h] *Servicio de Medicina Física y Rehabilitación, Hospital Universitario 12 de Octubre, Departamento de Radiología, Rehabilitación y Fisioterapia. Universidad Complutense de Madrid, Spain*
[i] *Hospital Santa Lucia-Cartagena, Cartagena, Spain*
[j] *Clínica Colman, Cádiz, Spain*

A B S T R A C T

Air pollution is a major cardiovascular risk factor leading to higher rates of heart failure and myocardial infarction (MI), but its effects on functional recovery after an MI remain unknown. Cardiac rehabilitation is a cornerstone of post-MI care and leads to better performance and quality of life, but its benefits may be hampered in heavily polluted environments. To assess the effect of different pollutants on post-MI rehabilitation, we included 137 post-MI patients from 7 Spanish hospitals that were enrolled in a cardiac rehabilitation program who underwent two cardiopulmonary exercise tests (CPET) within a 12-week period. Air pollution data were obtained from preexistent databases and matched with the patient's zip code. Patients exposed to higher NO2 levels (>22.5 ppb, above the median exposure of the cohort) had less improvement in peak oxygen consumption (0.9 % vs 9.5 %, p = 0.014), in oxygen pulse (0.0 % vs 6.9 %, p = 0.034) and tidal volume (−3.7 % vs 4.0 %). PM2.5 and PM10 did not have an impact on CPET parameters. After adjusting by age, sex, active smoking, hypertension, diabetes, hemoglobin, beta-blockers and left ventricular ejection fraction at discharge, the association between high NO2 levels and the change in peak VO2 remained significant (p = 0.029). This study highlights the importance of air pollution during cardiac rehabilitation and suggests that NO2 negatively impact on post-MI functional recovery.

1. Introduction

Air pollution is recognized as a major cardiovascular risk factor by the World Health Organization, as there is compelling evidence that air pollution increases the risk of myocardial infarction (MI), heart failure hospitalization and cardiovascular death, both in patients with history of cardiac disease and in those without [1,2]. In patients recovering from an MI, cardiac rehabilitation improves functional capacity and quality of life and accelerates recovery, enhancing the patient's physical and psychological readiness to restart

* Corresponding author. Servicio de Cardiología. Hospital Universitari Vall d'Hebron. Passeig Vall d'Hebron, 119-129, Barcelona, 08035, Spain.
E-mail address: jordi.baneras@vallhebron.cat (J. Bañeras).

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his usual activities [3,4]. From centuries ago, until nowadays, many physicians have advocated for staying away from the noise and pollution of the city to promote a faster and fuller recovery in a healthier environment, although there is compelling data suggesting the physical activity should be encouraged regardless of air pollution to decrease cardiovascular risk [5]. To date, however, there is little data to support this long-lasting recommendation.

2. Material and methodology

We conducted a retrospective, multicentric study including patients from 7 Spanish hospitals who suffered an MI between January 2015 and December 2019 who were enrolled into a cardiac rehabilitation program and had 2 cardiopulmonary exercise tests (CPET) within a 12-week period. By measuring oxygen consumption and carbon dioxide production during exercise, a CPET is the ideal instrument to assess cardiorespiratory fitness and identify the mechanism of exercise intolerance. Based on the zip code, the daily average concentration of air pollutants during the 2 previous years in the closest air pollution station to the patient zip code was collected from publicly available sources managed by the Spanish Department of Environmental Quality. Data was provided by the Air Quality Area from the Spanish Ministry for the Ecologic Transition. The pollutants that we included were nitrogen dioxide -NO2-, particulate matter 2.5 -PM2.5- and particulate matter 10 -PM10-, and if no data regarding air pollutant was available within a radius of 1 km from the boundaries of the zip code, the patient was excluded from the analysis. The CPET protocol varied from center to center, but most centers reported peak oxygen consumption (VO2 peak), oxygen uptake efficiency slope (OUES), oxygen pulse (VO2/heart rate) and the minute ventilation (VE)/minute CO2 production (VCO2) as a measure of ventilatory efficiency. Categorical values are presented as count and percentages, and continuous variables as median and interquartile ranges (IQR). were compared using Mann Whitney *U* test. Given the small sample size and significant P values in the Shapiro-Wilk test, all comparisons between medians and percentual changes in continuous variables were performed using Mann Whitney's *U* test, and adjusted analyses by were performed using multiple linear regression using CPET variables as the dependent variable. All analyses were performed using Stata 15.0 for Mac (StataCorp, TX, US), and a two-tailed P value < 0.05 was considered significant for all comparisons. Ethics approval was obtained (PR (AG)97/2020) from the Research Ethics Board of Vall d'Hebron University Hospital.

Table 1
Median values for several CPET parameters are provided depending on the average exposure to NO2, PM10 or PM2.5. The median values at baseline (CPET 1) and after finishing cardiac rehabilitation (CPET 2) are provided, along the individual change, calculated as the median percentual change compared to baseline ([CPET 2 – CPET 1]/CPET 1). The P value compared the median percentual change between groups using U-Mann Whitney test (above vs below median for each pollutant).

NO2							
	NO2 < median (n = 56*)			NO2 > median (n = 55*)			P value
	CPET 1	**CPET 2**	**% Diff**	**CPET 1**	**CPET 2**	**% Diff**	
VO2 peak (ml/kg/min)	21.0	23.3	9.5	19.0	20.6	0.9	0.014
% of predicted OUES	84.0	86.0	5.8	79.6	79.0	0.0	0.07
METS	6.1	6.8	9.1	5.7	6.3	1.5	0.09
O2 pulse (ml/heartbeat)	13.0	14.0	6.9	13.2	13.9	0.0	0.034
VE/VCO2 slope	30.5	29.9	−1.5	29.4	28.3	1.2	0.11
Tidal volume (L)	2.0	2.2	4.0	2.1	2.1	−3.7	0.010
PM10							
	PM10 < median (n=33*)			**PM10 > median (n=33*)**			**P value**
	CPET 1	**CPET 2**	**% Diff**	**CPET 1**	**CPET 2**	**% Diff**	
VO2 peak (mL/kg/min)	21.0	23.0	9.5	23.0	23.5	1.9	0.23
% of predicted OUES	94.0	91.8	7.1	95.0	96.4	1.8	0.68
METS	6.1	6.8	9.9	7.0	7.4	4.0	0.87
O2 pulse (mL/heartbeat)	13.2	14.0	1.6	14.7	16.3	5.9	0.16
VE/VCO2 slope	31.0	29.0	−4.7	28.7	29.7	−1.5	0.09
Tidal volume (L)	2.4	2.4	0.8	2.3	2.3	0.6	0.58
PM2.5							
	PM2.5 < median (n=21*)			**PM2.5 > median (n=19*)**			**P value**
	CPET 1	**CPET 2**	**% Diff**	**CPET 1**	**CPET 2**	**% Diff**	
VO2 peak (mL/kg/min)	20.0	23.0	4.3	19.0	23.0	3.3	0.84
% of predicted OUES	95.5	92.0	6.3	93.0	99.9	−0.3	0.93
METS	6.0	6.8	11.3	6.0	7.2	0.0	0.35
O2 pulse (mL/heartbeat)	13.2	13.7	3.3	13.0	14.4	1.2	0.95
VE/VCO2 slope	28.6	27.9	−0.8	31.1	29.9	−0.3	0.48
Tidal volume (L)	2.4	2.4	−5.0	2.3	2.3	4.9	0.030

CPET: cardiopulmonary exercise test; NO2: nitrogen dioxide; VO2: oxygen consumption; OUES: oxygen uptake efficiency slope; VE/VCO2: minute ventilation/minute CO2 production. *Number of patients with valid values.

3. Results

A total of 137 patients were included. Median age was 59 (interquartile range 50–65) years old, and 15 (11 %) were women. There were 52 (38.0 %) patients with hypertension and 28 (20.6 %) with diabetes, and 11 (8.0 %) had been previously admitted due to heart failure. The median ejection fraction after the MI was 50 % (IQR 44 %–60 %). Cardiac rehabilitation had a positive impact in the overall cohort, with a significant increase in peak VO2 (20 ml/kg/min at baseline vs 23 ml/kg/min at the second CPET, $p < 0.001$), oxygen pulse (13.5 vs 14.1 ml O2 per heartbeat) and more METS (6.0 vs 6.6, $p < 0.001$), with no change in VE/VCO2 slope ($p = 0.24$) nor in tidal volume ($p = 0.06$).

Based on the WHO recommendations, median yearly exposure was above the suggested threshold for cardiovascular risk in 98.4 % of the patients for NO2, in 100 % for PM10 and in 69 % for PM2.5, therefore not allowing to create groups for comparison, so that patients were divided based on the median exposure to each of the pollutants. High NO2 levels (>22.5 parts per billion) was significantly associated with an impaired recovery after an MI, with only a 0.9 % increase in VO2 peak compared to 9.5 % increase in patients in the low NO2 group ($p = 0.014$). Patients exposed to high NO2 levels also improved their oxygen pulse less (0.0 % vs 6.9 %, $p = 0.034$), as well as their tidal volume (−3.7 % vs 4.0 %, $p = 0.010$), with a trend towards less METS exercised ($p = 0.09$) and worse % of the predicted OUES ($p = 0.07$)(see Table 1) After adjusting by age, sex, active smoking, hypertension, diabetes, hemoglobin, beta-blockers and left ventricular ejection fraction at discharge, the association between high NO2 levels and the change in peak VO2 remained significant ($p = 0.029$), whereas the association with oxygen pulse and tidal volume did not. These results were not seen when patients were divided based on PM10 median exposure, not when divided depending on average PM2.5 levels.

4. Discussion

This study is the first to suggest that air pollution may hamper the recovery after an MI by undermining the beneficial effects of cardiac rehabilitation and emphasizes the need to conduct further research to determine the effects of air pollution on cardiac remodeling and functional recovery in patients with cardiac disease. Specifically, we observed that patients exposed to higher NO2 levels had less improvement in VO2 peak after adjusting by several confounders. The causal association between NO2 and impaired recovery after an MI is yet to be stablished of prospective studies, ideally measuring individual exposure to several pollutants, but we believe it is worth exploring as it appears to be hypothesis generating. We exclusively assessed average air pollution in the two years preceding the MI, but we did not consider exposure to air pollution after the MI and during the recovery phase, which might have yielded to different results than the ones we observed.

Of note, the average pollution in the patient zip code was obtained from a national database and may not reflect the precise levels of pollutant that the patients were exposed to, and this work is therefore subjected to the limitations intrinsic to ecological studies. Also, the average values for air pollutants were above the WHO recommendations, and bigger differences may have been observed had the control group been exposed to air pollutant levels below the recommended WHO thresholds. Sample size is another major limitation of the study, which was due to lack of available measurements of certain pollutants, excessive distance between the zip code and pollution station and heterogeneity in CPET protocols between centers. Despite the known effects of SO2 in cardiovascular risk [6], no data was reported in this study related to SO2 given the small numbers of patients for whom we could obtain the concentrations of these pollutants at less than 1 km radius from their zip code. However, the associations between NO2, PM10 and PM2.5 and cardiovascular risk are stronger than those observed with SO2 or ozone [7].

5. Conclusions

Patients living in areas with higher exposure to NO2 levels during the two years preceding an MI had a worse recovery during a cardiac rehabilitation program, with an impaired increase in peak VO2 at the end of the training program after adjusting for several confounders. This suggests a deleterious effect of air pollution on functional recovery after an MI and warrants further research.

CRediT authorship contribution statement

Jordi Bañeras: Writing – review & editing, Writing – original draft, Validation, Investigation, Formal analysis, Data curation, Conceptualization. **Alejandro Berenguel-Senén:** Writing – review & editing, Resources, Investigation, Data curation. **Eulogio Pleguezuelos:** Writing – review & editing, Resources, Investigation. **José Antonio Alarcón:** Writing – review & editing, Resources, Investigation, Data curation. **Jesús Vallejo:** Writing – review & editing, Resources, Methodology. **Paz Sanz-Ayán:** Writing – review & editing, Resources, Investigation. **Juan Izquierdo-García:** Writing – review & editing, Resources, Investigation. **José Garcia:** Writing – review & editing, Resources, Investigation. **Rafael Colman:** Writing – review & editing, Resources, Investigation. **Juan Ignacio Castillo-Martín:** Writing – review & editing, Resources, Investigation. **Eduard Ródenas-Alesina:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation, Conceptualization.

Data availability statement

Data will be available upon reasonable request to the corresponding author.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e40929.

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