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Impact of residential greenness on myocardial infarction in the population with diabetes: A sex-dependent association?



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ABSTRACT

Living in urban areas with abundant greenness might provide health benefits in general population. Literature suggests that sex/gender plays a role in the association between greenness and health outcomes. But the impact of greenness in populations with moderate to high cardiovascular risk, such as persons with diabetes, is still unknown. Our aim was to evaluate the relationship between urban greenness and myocardial infarction incidence in persons with type 2 diabetes in Barcelona (Catalonia, Spain), and seek potential gender/sex differences in this association.

This retrospective cohort study is based on data from the System for the Development of Research in Primary Care (SIDIAP database). We used Cox models to estimate if a 0.01 increase in Normalized Difference Vegetation Index (NDVI) at census tract level was associated to reduced risk of developing a myocardial infarction. Models were adjusted by demographic and clinical characteristics at individual level, and by environmental and socioeconomic variables at census tract level. Amongst 41,463 persons with diabetes and 154,803.85 person-years of follow-up, we observed 449 incident cases of acute myocardial infarction. For each 0.01 increment in NDVI the risk of developing a myocardial infarction decreased by 6% (Hazard Ratio, HR = 0.94; 95%CI, 0.89-0.99) in the population with diabetes. When stratifying by sex, we observed a significant association only in men (HR = 0.91; 95%CI, 0.86-0.97).

People with diabetes living in urban greener areas might benefit from reduced cardiovascular risk, specially men. We observed sex/gender disparities, which could be related to different exposures and activities performed in green spaces between men and women. Further studies are needed to confirm sex/gender disparities between greenness exposure and cardiovascular outcomes. Our findings contribute to improve the health of people with diabetes who should be recommended to spent time and exercise in green areas.

1. Introduction

Cardiovascular diseases (CVD) are a leading cause of death, accounting for 18 million deaths each year worldwide (Mendis et al., 2011). Over the last decades, CVD mortality has declined in Western countries due to a combination of pharmacological treatments and primary prevention plans, but it is still high in many other countries (Mendis et al., 2011). Prevention of CVD mainly focuses on lifestyles, demographic characteristics, genetic disorders, or pathophysiological risk factors. But prevention based on other risk factors, such as environmental exposures, remains incipient. Environmental exposures might directly affect cardiovascular risk (Ponjoan et al., 2017, 2020), but also might contribute to modify lifestyles (Hobbs et al., 2020; Martins et al., 2021).

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The environment for 55% of the world's current population involves the urban areas they inhabit, and such percentage is projected to increase to 75% in 2050 (United Nations, Department of Economic and Social Affairs, 2019). Urbanization impacts human health through multiple processes such as heat island effects, pollution, or climate change (Lee and Maheswaran, 2011; Tonne et al., 2021). But emerging evidence suggests that living in urban areas with abundant greenness nearby -such as parks, gardens, or patches covered by trees or vegetation - may reduce mortality (Gascon et al., 2016; Nieuwenhuijsen et al., 2018; Rojas-Rueda et al., 2019), and protect against depression, asthma, or cardiovascular outcomes (Fong et al., 2018; James et al., 2015). The mechanisms through which greenness may promote health might include stress reduction (Triguero-Mas et al., 2017), promotion of social interactions (Maas et al., 2009), increase in physical activity (Lu et al., 2018), and reduction in noise levels (Dzhambov and Dimitrova, 2014), air pollution (Crouse et al., 2019), or heat (Bowler et al., 2010). Moreover, exposure to greenness has been associated with lower levels of sympathetic activation, reduced oxidative stress, and higher angiogenic capacity (Yeager et al., 2018).

Most studies have assessed the benefits of urban greenness on cardiovascular health in general population (Jennings et al., 2019; Orioli et al., 2019; Seo et al., 2019; Wang et al., 2019; Yitshak-Sade et al., 2019), and some of them have suggested sex or gender differences in the association between greenness and human health (Bolte et al., 2019). The analysis of cardiovascular outcomes have reported sex or gender differences mainly due to variations in the social use of green spaces, frequency of visits, and safety perception, or in time spent outdoors around the neighborhood (Plans et al., 2019; Richardson and Mitchell, 2010).

However, the impact of greenness on specific targeted populations with moderate to high cardiovascular risk, such as diabetic patients, remains unknown. We found only one publication that assessed the role of greenness on the cardiovascular health of people with type 2 diabetes, and observed no significant associations (Astell-Burt et al., 2021).

Patients with diabetes are a targeted group in primary prevention of CVD because they are, on average, at double the risk of CVD compared to the general population (Sarwar et al., 2010). To reduce such increased cardiovascular risk in diabetic patients, clinical guidelines recommend managing lifestyles - improving diet and engaging in regular physical exercise -and controlling glucose by reducing glycated hemoglobin levels (Piepoli et al., 2016). Some evidence supports the association of higher exposure to greenness with lower levels of glucose (Yang et al., 2019) and reduced diabetes prevalence in the general population (Fan et al., 2019), with different effects in men and women (Yang et al., 2019). Therefore, we hypothesized that higher levels of exposure to greenness might reduce the risk of cardiovascular disease in persons with diabetes, and that this association would differ between men and women. We aimed to evaluate the relationship between urban greenness and myocardial infarction incidence in persons with diabetes mellitus who lived in the city of Barcelona (Catalonia, Spain). Additionally, we will examine sex differences in such association.

2. Material and methods

This retrospective cohort study was approved by the Ethics Committee from the Fundació Institut Universitari per a la recerca a l'Atenció Primària de Salut Jordi Gol i Gurina (IDIAPJGol) (code: P15/072).

2.1. Study population and follow-up

We included persons with diabetes who were registered in the System for the Development of Research in Primary Care (SIDIAP database) (Bolíbar et al., 2012), which is a database specifically designed for biomedical research. SIDIAP contains pseudonymized longitudinal medical records of 6 million patients attended by the Catalan Institute of Health (80% of the Catalan population and 12% of the Spanish

population). SIDIAP comprises clinical and referral events registered in electronic medical records, including comprehensive demographic information, clinical diagnoses, or tests. Diagnostic codes are recorded in SIDIAP using the *International Classification of Diseases, 10th revision* (ICD-10), and pharmacological treatments using the *Anatomical Therapeutic Chemical Classification System* (ATC codes). SIDIAP data is representative of the population of Catalonia in terms of geographic, age, and sex distributions (García-Gil et al., 2011), and records of cardiovascular risk factors and diseases had been externally validated (Ramos et al., 2012).

We identified diabetic persons as those who had a diagnosis for type 2 diabetes mellitus (ICD-10 codes: E11). We included persons aged at least 18 years old, who lived in the city of Barcelona (Catalonia, Spain), and were registered in SIDIAP on January 1, 2011. We excluded persons with a previous history of cardiovascular disease (ICD-10 codes: I20–I25, I60–I64, G45-G46, I73, I50, I11.0, I13.0, I13.2).

Follow-up started on January 1, 2011, and censoring was applied at the earliest of the following events: death, transfer from SIDIAP, acute myocardial infarction, or end of the study period (December 31, 2014).

2.2. Variables

Exposure was the abundance of greenness, in particular, the Normalized Difference Vegetation Index (NDVI) within an area that included not only the census tract, but also a buffer of 300 m around the census tract. The NDVI is an indicator based on the difference between visible red and near-infrared surface reflectance; values range from -1 to +1, with higher values indicating more greenness (NASA, 2000). NDVI data were obtained from the Landsat 8 satellite. We used cloud-free images at a spatial resolution of 30 m during the greenest season (April to July) to obtain annual estimates of NDVI during 2010–2014.

The outcome was first ever occurrence of acute myocardial infarction recorded in the SIDIAP database (ICD-10 codes: I21–I23). The outcome was measured at individual level, as well as the following covariates: age, sex (women, men), body mass index (kg/m²), hypertension (ICD-10 codes: I10–I13, H35), dyslipidemia (ICD-10 codes: E78), and tobacco consumption (smoker, ex-smoker and non-smoker). Covariates at census tract level included deprivation MEDEA index (Domínguez-Berjón, 2008) – which has proven predictive validity (García-Gil et al., 2014) - and the following environmental variables (Nieuwenhuijsen et al., 2018): air pollution (mean annual concentrations (μ g/m³) of PM_{2.5} and NO₂); daytime traffic noise levels, estimated using the Barcelona's strategic noise map (700–2300 h; LAeq 16 h) (Generalitat de Catalunya, 2012); and walkability, using a self-made normalized score with population density, street connectivity, and land use composite as indicators (-4.8 - 11.5) (Frank et al., 2006).

From each individual, we obtained the census tract of their residence. Clinical data at individual level was linked with exposure and other environmental variables measured at census tract level. There were 1061 census tracts in Barcelona, with a median size of 3.6 ha and a mean population of 1523 inhabitants.

2.3. Statistical analyses

We described categorical and continuous variables using absolute and relative frequencies, and mean and standard deviation, respectively. We calculated the Pearson correlation coefficient and we drew scatter plots to study collinearity between continuous variables. Furthermore, we performed mediation analyses to quantify the contribution of a given variable as mediator of the association between residential greenness and incidence of myocardial infarction. In particular, we considered hypertension, dyslipidemia, body mass index, air pollution, and noise as potential mediators because some studies reported them as mediators between greenness exposure and health outcomes (Huang et al., 2020; Orioli et al., 2019; Yitshak-Sade et al., 2017). We assessed mediation effects using the approach proposed by Baron and Kenny (1986), which includes three models: 1) Y = X; 2) M = X; 3) Y = X + M, where Y is the outcome (myocardial infarction), X is the independent variable (NDVI), and M is the mediator (BMI, dyslipidemia, hypertension, concentration of PM_{2.5}, concentration of NO₂, or noise) (Supplementary Figure 1). Possible mediators were tested one at a time. We considered that a variable was a mediator when it could be part of the causal chain. Significant associations were observed in the second and third models, and the magnitude of the association between NDVI and myocardial infarction in the first model was higher than in the third.

We used Cox proportional hazards regression models with timedependent exposures to estimate associations between annual greenness indicators and cardiovascular diseases. First, we calculated unadjusted hazard ratios (HRs); then, we calculated adjusted HRs by sequentially adding the following covariates: age and sex (model A), deprivation (model B); hypertension, dyslipidemia, body mass index, and tobacco consumption (model C); and finally we added all environmental variables (annual geometric mean concentration of PM2.5 (µg/ m^3), annual geometric mean concentration of NO₂ ($\mu g/m^3$), geometric mean of daytime noise level (5 dB(A)), and walkability). The proportionality of hazards assumption was tested. We ran models including the interaction term (0.01 NDVI increase *sex) for the whole study population and we also stratified the models by sex. We conducted sensitivity analyses by excluding people who changed their residency to another census tract during follow-up. Statistical significance was considered at p-values < 0.05. All data analyses were conducted using the package R Core Team (2020) (R Development Core Team, 2018).

3. Results

We identified 41,463 persons who had a diagnosis of type 2 diabetes mellitus recorded in SIDIAP on January 1, 2011. Non-smokers and patients with hypertension were predominant in the study; mean age was 68.8 years (SD, 11.9). A detailed description of the demographic characteristics, cardiovascular risk factors and environmental variables are shown in Table 1.

Over approximately 154,803.85 person-years of follow-up, we observed 449 incident cases of acute myocardial infarction, with an incidence rate of 29 per 10,000 person-years. Within women, we observed 154 cases during 77,769.35 person-years of follow-up, and the incidence rate was 19.8 per 10,000 person-years; the corresponding figures for men were 295 cases in 77,034.5 person-years of follow-up, and the incidence rate was 38.29 per 10,000 person-years.

Greenness abundance at census tract level was generally low: geometric mean of NDVI was 0.13; and quartiles 1 and 3 for NDVI were 0.12 and 0.15, respectively. Traffic noise and air pollution levels were much higher than those in the WHO guidelines (Table 1). The correlation between the different exposure variables and some of the covariates was generally low to moderate, with some exceptions (Table 2). Mediation analyses provided no significant results (Supplementary Table 1), which indicated that, in our study, the association between greenness abundance and incidence of myocardial infarction might not be mediated by any of the evaluated covariates. In this diabetic population, we observed that each 0.01 increment of NDVI was associated with a 6% decrease (HR = 0.94; 95%CI 0.89–0.99) in the fully-adjusted risk of developing a myocardial infarction (Table 3). Detailed results of the fully-adjusted model are shown in the Supplement (Supplementary Table 2). Results of models sequentially adjusted by demographic characteristics, cardiovascular risk factors, and environmental variables are provided in Table 3. The interaction between sex and NDVI increase was not significant (P > 0.544).

When stratifying by sex, we observed a significant effect only in men: in the fully-adjusted model the HR was 0.91 (95%CI 0.86–0.97) in men and 0.99 (95%CI 0.92–1.08) in women (Table 3). Detailed results of the full-adjusted models stratified by sex are shown in the Supplementary Table 2. In women, none of the models showed significant results

Table 1

Ľ	escription	of	clinical	and	environmenta	al	variable	es.
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$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Variables	All Population	Women	Men	
Health factors Age, mean(sd) 68.8 (11.9) 71.0 (11.6) 66.6 (11.8) Smoking, $n(%)$ Never-Smokers 28,506 (68.8%) 17,769 (85.6%) 10,737 (51.9%) Smokers 6685 (16.1%) 1666 (8.0%) 5019 (24.2%) Ex-Smokers 6272 (15.1%) 1323 (6.4%) 4949 (23.9%) Deprivation MEDEA index, $n(%)$ 1 11,203 (27.0%) 5293 (25.5%) 5910 (28.5%) 1st Quintile 10,609 (25.6%) 5223 (25.2%) 5386 (26.0%) 3rd Quintile 3rd Quintile 7352 (17.7%) 3740 (18.0%) 3612 (17.4%) 4th Quintile 6160 (14.9%) 3220 (15.5%) 2940 (14.2%) 5th Quintile 6139 (14.8%) 3282 (15.8%) 2857 (13.8%) Dyslipidemia, $n(%)$ 20,314 (49.0%) 10,847 (52.3%) 9467 (45.7%) Hypertension, $n(%)$ 27,334 (65.9%) 14,856 (71.6%) 12,478 (60.3%)	Variables				
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Never-Smokers 28,506 (68.8%) 17,769 (85.6%) 10,737 (51.9%) Smokers 6685 (16.1%) 1666 (8.0%) 5019 (24.2%) Ex-Smokers 6272 (15.1%) 1323 (6.4%) 4949 (23.9%) Deprivation MEDEA index, n(%) 5293 (25.5%) 5910 (28.5%) 1st Quintile 11,203 (27.0%) 5293 (25.5%) 5386 (26.0%) 3rd Quintile 7352 (17.7%) 3740 (18.0%) 3612 (17.4%) 4th Quintile 6160 (14.9%) 3220 (15.5%) 2940 (14.2%) 5th Quintile 6139 (14.8%) 3282 (15.8%) 2857 (13.8%) Dyslipidemia, n(%) 20,314 (49.0%) 10,847 (52.3%) 9467 (45.7%) Hypertension, n(%) 27,334 (65.9%) 14,856 (71.6%) 12,478 (60.3%)		68.8 (11.9)	71.0 (11.6)	66.6 (11.8)	
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$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Never-Smokers	28,506 (68.8%)	17,769 (85.6%)	10,737 (51.9%)	
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Smokers	6685 (16.1%)	1666 (8.0%)	5019 (24.2%)	
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Ex-Smokers	6272 (15.1%)	1323 (6.4%)	4949 (23.9%)	
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Deprivation MEDEA index,	n(%)			
$\begin{array}{llllllllllllllllllllllllllllllllllll$	1st Quintile	11,203 (27.0%)	5293 (25.5%)	5910 (28.5%)	
$\begin{array}{llllllllllllllllllllllllllllllllllll$	2nd Quintile	10,609 (25.6%)	5223 (25.2%)	5386 (26.0%)	
$\begin{array}{llllllllllllllllllllllllllllllllllll$	3rd Quintile	7352 (17.7%)	3740 (18.0%)	3612 (17.4%)	
$\begin{array}{llllllllllllllllllllllllllllllllllll$	4th Quintile	6160 (14.9%)	3220 (15.5%)	2940 (14.2%)	
Hypertension, n(%) 27,334 (65.9%) 14,856 (71.6%) 12,478 (60.3%)	5th Quintile	6139 (14.8%)	3282 (15.8%)	2857 (13.8%)	
	Dyslipidemia, n(%)	20,314 (49.0%)	10,847 (52.3%)	9467 (45.7%)	
Body Mass Index, mean(sd) 30.0 (5.1) 30.9 (5.6) 29.2 (4.3)	Hypertension, n(%)	27,334 (65.9%)	14,856 (71.6%)	12,478 (60.3%)	
	Body Mass Index, mean(sd)	30.0 (5.1)	30.9 (5.6)	29.2 (4.3)	
Years since diagnosis of 6.2 (5.1) 6.4 (5.2) 5.9 (5.0)	Years since diagnosis of	6.2 (5.1)	6.4 (5.2)	5.9 (5.0)	
diabetes, mean(sd)	diabetes, mean(sd)				
Environmental factors	Environmental factors				
NDVI, _{GM(Q1-Q3)} 0.13 0.13 0.13	NDVI, GM(Q1-Q3)	0.13	0.13	0.13	
(0.12–0.15) (0.12–0.15) (0.12–0.15)		(0.12-0.15)	(0.12-0.15)	(0.12-0.15)	
Mean annual 52.65 52.54 52.76	Mean annual	52.65	52.54	52.76	
concentration of NO ₂ (47.63–59.19) (47.59–59.20) (47.68–59.18)	concentration of NO2	(47.63–59.19)	(47.59–59.20)	(47.68–59.18)	
$(5 \ \mu g/m^3), \ _{GM(Q1-Q3)}$	$(5 \ \mu g/m^3), \ _{GM(Q1-Q3)}$				
Mean annual 15.90 15.87 15.92		15.90	15.87	15.92	
concentration of PM _{2.5} (14.84–17.56) (14.83–17.51) (14.85–17.60)	concentration of PM _{2.5}	(14.84–17.56)	(14.83–17.51)	(14.85–17.60)	
$(5 \ \mu g/m^3), \ _{GM(Q1-Q3)}$	$(5 \ \mu g/m^3), \ _{GM(Q1-Q3)}$				
Daytime noise average 64.16 64.05 64.27	Daytime noise average	64.16	64.05	64.27	
level (5 dB(A)), _{GM(Q1} . (61.79–66.78) (61.71–66.66) (61.91–66.88)	level (5 dB(A)), GM(Q1-	(61.79-66.78)	(61.71-66.66)	(61.91-66.88)	
03)					
Walkability, _{GM(Q1-Q3)} 1.53 1.56 1.50		1.53	1.56	1.50	
(-0.80-2.30) (-0.80-2.30) (-0.80-2.30)		(-0.80-2.30)	(-0.80-2.30)	(-0.80-2.30)	

GM(Q1-Q3): geometric mean (quartile 1 – quartile 3).

Table 2

Correlation matrix for environmental variables.

	NDVI	PM _{2.5}	NO_2	Traffic Noise	Walkability
NDVI	1.0	-0.600	-0.557	-0.258	-0.476
PM _{2.5}	-0.600	1.0	0.818	0.418	0.252
NO ₂	-0.557	0.818	1.0	0.309	0.332
Traffic Noise	-0.258	0.418	0.309	1.0	0.020
Walkability	-0.476	0.252	0.332	0.020	1.0

(Table 3).

Sensitivity analyses were conducted by restricting the population to those who did not move to another census tract during the follow-up (n = 40,804) – that is, excluding 659 movers. Sensitivity analyses showed consistent results (Supplementary Table 3).

4. Discussion

This is the first study to report that persons with diabetes living in cities might benefit from high levels of residential greenness. In particular, we observed that increasing NDVI levels were associated with a risk reduction in the incidence of acute myocardial infarction in persons with diabetes. Furthermore, we observed that the potential benefits of greenness differed between sexes: the association between greenness and incidence of myocardial infarction was significant only in men.

Literature about the effect of greenness in the diabetic population is currently limited to one single study conducted in Australia. The authors observed a non-significant risk reduction of acute myocardial infarction of 3%, related to a 10% increase in tree canopy (Astell-Burt et al., 2021). Therefore, our results provide a novel contribution because we found significance in the associations between higher levels of NDVI and a reduced risk of myocardial infarction. Moreover, our findings are in line with one study conducted in Israel that reported a negative association

Table 3

Hazard ratios (95% confidence intervals) for a 0.01 increase in NDVI.

Population	Unadjusted	Adjusted models					
	models	Model A (adjusted by age and/ or sex)	Model B (Model A + deprivation)	Model C (Model $B + CV$ risk factors ^a)	Model D (Model C $+$ environmental variables ^b)		
Entire population	0.97 (0.94–1.00)	0.97 (0.94–1.00)	0.97 (0.93–1.00)	0.97 (0.94–1.00)	0.94 (0.89–0.99)		
Women	0.98 (0.93-1.03)	0.98 (0.93-1.04)	0.98 (0.93-1.04)	0.98 (0.93-1.04)	0.99 (0.92–1.08)		
Men	0.96 (0.92–1.01)	0.96 (0.92–1.01)	0.96 (0.92–1.01)	0.96 (0.92–1.01)	0.91 (0.86–0.97)		

^a Cardiovascular risk factors included: hypertension, body mass index, dyslipidemia, and tobacco consumption.

^b Environmental variables included: mean annual concentration of $PM_{2.5}$ (µg/m³), mean annual concentration of NO₂ (µg/m³), daytime noise average level (5 dB (A)), and walkability.

between NDVI and the onset of myocardial infarction (odds ratio = 0.72; 95%CI 0.61–0.85) in patients with at least one cardiovascular risk factor (dyslipidemia, diabetes, hypertension, or smoking habit) (Yitshak-Sade et al., 2017).

The association between greenness and reduced onset of cardiovascular disease (Nieuwenhuijsen et al., 2017; Richardson and Mitchell, 2010; Thiering et al., 2016) has been explained by the benefits of both direct and indirect effects of exposure to green vegetation. Direct effects of greenness have been related to the innate biophilic tendencies of human beings to seek connections with nature and non-human life (Yeager et al., 2019). Indirect effects have been related to the presence of mediator effects, such as stress reduction, social cohesion, sunlight exposure, or physical activity (Groenewegen et al., 2012; Jia et al., 2018). Some of the mediator effects might be of special relevance for the diabetic population. For example, physical activity is one of the main goals in the management of diabetes. In the primary care centers of the Catalan Institute of Health, patients with diabetes are formally advised to engage in moderate exercise, such as walking or cycling at least 150 min per week (Mata et al., 2013). In fact, in Spain, the population with diabetes showed higher levels of physical activity than the general population, mainly attributed to their more frequent walks (Murillo et al., 2008). In urban environments, patients with diabetes or cardiovascular conditions used parks more frequently than healthy people, suggesting that they might be more exposed to greenness than the general population (Lee, 2018).

We found that the association between greenness and reduced risk of myocardial infarction was significant in men, but not in women. As the interaction term was not significant, one may argue that these results could be due to a low powered sample size in women or a chance significant result in men. However, a sex-and-gender dependent association between greenness and cardiovascular health could be explained by three main mechanisms. First, the reduction in the risk of developing a myocardial infarction might be stronger in high-risk groups. The cardiovascular guidelines for clinical practice state that individuals at highest risk gain the most from preventive efforts (Piepoli et al., 2016). In line with previous literature, we found that the incidence of myocardial infarction in men doubled the incidence in women (Lopez-de-Andres et al., 2021), and thus they might achieve higher risk reduction from being exposed to greenness than women. Other studies have also reported higher benefits of greenness exposure in men; in particular, the associations between fasting glucose or fasting insulin and greenness were stronger in men than in women according to a study in Chinese general population (Yang et al., 2019). Second, exposure to greenness might be lower in women than in men in our study area. We used residential greenness as exposure, which has been related to park use -people living closer to the park tend to visit it more often (Cohen et al., 2007; Richardson and Mitchell, 2010). Evidence suggests that men are more exposed to greenness because they visit parks more often than women (Cohen et al., 2007; Evenson et al., 2016). In Barcelona, a study estimated that 55% of park visitors were men, and the remaining 45% were women (Pérez-Tejera et al., 2018); even though, according to the census, 47% of the citizens in Barcelona are men and 53% are women.

Women might visit parks less often, partly due to acute concerns about their personal safety when visiting green spaces on their own (Richardson and Mitchell, 2010), which seems to explain why women tend to visit parks in groups (Pérez-Tejera et al., 2018). Third, activities performed in the green areas might differ between men and women. Men tend to spend more time doing physical activity when visiting parks (Derose et al., 2018), whilst most women use parks mainly following the traditional gender role as caregivers of children and/or elders (Cohen et al., 2007). In Barcelona, men not only are more physically active when visiting parks (18.9% vs 11.8%), but also perform more vigorous exercises than women (14.1% vs 1.8%) (Pérez-Tejera et al., 2018). Women tend to go to the parks more often after school has finished, they are more likely to be close to playground areas, and more frequently involved in groups with children, adolescents, or elders (Pérez-Tejera et al., 2018).

Our results indicate that the association between greenness abundance and incidence of myocardial infarction was not mediated by other variables. This finding is in line with other studies that neither detected any mediation of BMI (Xie et al., 2020), air pollution (Jimenez et al., 2020), or traffic noise (Dzhambov et al., 2018) in the association between greenness and different health outcomes. But literature provides controversial results; other analysis identified BMI, air pollution (Asta et al., 2021), dyslipidemia (Yitshak-Sade et al., 2017), physical activity (Dadvand et al., 2016), or hypertension (Yang et al., 2020) as mediators when studying the relationship between greenness and health outcomes. Therefore, more studies are needed to better understand the pathways involved in the relationship between greenness and myocardial infarction, especially in high cardiovascular risk populations such as people diagnosed with diabetes, and including considerations for men and women.

We found an unexpected inverse association between the concentration of $PM_{2.5}$ and the incidence of myocardial infarction. This result disagrees with previous consistent evidence on the positive association between the concentration of $PM_{2.5}$ and the risk of suffering myocardial infarction and other cardiovascular outcomes (Yang et al., 2021). Residual confounding of unmeasured variables could explain the inverse association detected in our analysis.

This study has several strengths. One is its large sample size (more than 40,000 persons), which is highly representative of the diabetic population. Even more, we used NDVI satellite data to assess greenness, to provide updated data on green vegetation abundance within the follow-up period. Finally, we adjusted for both the main cardiovascular risk factors and the main environmental variables related to air pollution, traffic noise, and walkability.

We acknowledge some study limitations. First, there could be some residual confounding due to unobserved variables or eventual mediators such as physical activity (Dadvand et al., 2016). Second, exposure to greenness was not assessed at individual level and therefore we could not consider time spent in greenspaces or frequency of visits. However, we assessed greenness at a census tract level, which is a method that has been successfully implemented in several studies (i.e. (Nieuwenhuijsen et al., 2018; Wang et al., 2019; Yitshak-Sade et al., 2017). Third, NDVI

provided data about abundance of greenness, but it is not informative about the type or quality of vegetation, which have been reported to provide health benefits (van den Berg et al., 2015). Fourth, we used a unique 300-m buffer to assess greenness abundance. The size of the buffer used to assess greenness abundance could affect the strength of the association between greenness and the health outcome (Klompmaker et al., 2018), but we did not have information on several buffers.

Our findings indicate that general practitioners and nurses could encourage patients diagnosed with diabetes living in urban environments to spent time outdoor and exercise in areas with green vegetation. These recommendations would contribute to improve their health and reduce the huge economic burden of diabetes in the public health systems. Besides, our findings highlight the importance of not assuming sex or gender equality regarding the health benefits of greenness, and calls to explore specific biological differences between sexes, as well as specific necessities in both genders - or even to consider non-binary genders. We recommend expanding and connecting areas with green vegetation within cities, and making them accessible and safe in terms of security for both men and women. Further research is needed to better understand the effect of greenness in patients with diabetes and, in particular, the role of physical activity in this association. The significant associations between greenness abundance and myocardial infarction only in men should also be further assessed. We hypothesized that this might be partially explained by the higher cardiovascular risk in men. The question arises as to whether a similar tendency - that is, stronger associations between greenness and myocardial infarction in groups with higher cardiovascular risk - occurs in other populations, for example, in persons without diabetes.

5. Conclusions

We conclude that persons diagnosed with type 2 diabetes mellitus living in cities could benefit from reduced risk of acute myocardial infarction if their residence was surrounded by high levels of greenness. Furthermore, we observed that sex and/or gender might play a role in the relationship between greenness exposure and myocardial infarction incidence because the effect was significant only in men.

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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.envres.2021.112449.

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