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# **Impact of air pollution on hospital patients admitted with ST- and non-ST-segment elevation myocardial infarction in heavily polluted cities within the European Union**

**Running title:** Impact of air pollution on STEMI and NSTEMI admitted to hospital in heavily polluted cities within the EU

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## **Abstract**

**Background:** Air pollution triggered diseases have become a leading health problem worldwide. The main adverse effects of air pollutants on human health are related to the cardiovascular system and particularly show an increasing prevalence of myocardial infarct and stroke. The aim of the study was to evaluate the influence of main air pollutants on non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI) admissions to local interventional cardiology centers.

**Methods:** Between 2014 and 2015, a multicenter registry of 1957 patients with acute myocardial infarction (STEMI, NSTEMI) admitted to interventional cardiology departments

in three Polish cities were under investigation. The air pollution (PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub>) and weather conditions (temperature, barometric pressure, humidity) data for each city were collected as daily averages. The case-crossover design and conditional logistic regression were used to explore the association between acute myocardial infarctions and short-term air pollution exposure.

**Results:** Occurrence of NSTEMI on the day of air pollution was triggered by PM<sub>2.5</sub> (OR = 1.099,  $p = 0.01$ ) and PM<sub>10</sub> (OR = 1.078,  $p = 0.03$ ). On the following day after the air pollution was recorded, NSTEMI was induced by: PM<sub>2.5</sub> (OR = 1.093,  $p = 0.025$ ), PM<sub>10</sub> (OR = 1.077,  $p = 0.025$ ) and SO<sub>2</sub> (OR = 1.522,  $p = 0.009$ ). For STEMI, events that occurred on the day in which air pollution was triggered by: PM<sub>2.5</sub> (OR = 1.197,  $p < 0.001$ ), PM<sub>10</sub> (OR = 1.163,  $p < 0.001$ ), SO<sub>2</sub> (OR = 1.670,  $p = 0.001$ ) and NO<sub>2</sub> (OR = 1.287,  $p = 0.011$ ). On the following day after air pollution was recorded, STEMI was induced by: PM<sub>2.5</sub> (OR = 1.172,  $p < 0.001$ ), PM<sub>10</sub> (OR = 1.131,  $p = 0.001$ ), SO<sub>2</sub> (OR = 1.550,  $p = 0.005$ ) and NO<sub>2</sub> (OR = 1.265,  $p = 0.02$ ). None of the weather conditions indicated were statistically significant for acute myocardial infarction occurrence.

**Conclusions:** The most important pollutants triggering acute myocardial infarction occurrence in the population of southern Poland, both on the day of air pollution and the following day are particulate matters (PM<sub>2.5</sub>, PM<sub>10</sub>) and gaseous pollutants including NO<sub>2</sub> and SO<sub>2</sub>. These pollutants should be regarded as modifiable risk factors and thus, their reduction is a priority in order to decrease total morbidity and mortality in Poland.

**Key words:** air pollution, myocardial infarction, non-ST-segment elevation myocardial infarction (NSTEMI), ST-segment elevation myocardial infarction (STEMI)

## INTRODUCTION

Air pollution triggered diseases have become a leading problem both in well-developed and for emerging economy countries. According to The World Health Organization 3.7 million deaths per year occur from exposure to outdoor air pollution [1]. What is more, 72% of air pollution-related premature deaths were due to ischemic heart

disease and strokes [2]. This confirms, that the cardiovascular system is one of the most susceptible human body systems affected by ambient air pollution.

Outdoor air pollution is particularly driven by industry, transport (especially diesel engines) and other combustion processes such as heating and power generation devices. It consists of particulate matter (PMs) and gaseous pollutants — carbon monoxide (CO), sulfur dioxide (SO<sub>2</sub>), nitrogen dioxide (NO<sub>2</sub>) and ozone (O<sub>3</sub>). PMs can be further divided according to their diameter to PM<sub>10</sub> ( $\leq 10 \mu\text{m}$ ), PM<sub>2.5</sub> ( $\leq 2.5 \mu\text{m}$ ).

Previous studies have explored the association between acute myocardial infarctions (AMIs) and air pollution. The results were conflicting. Some of them have shown an association between AMIs and some air pollutants, especially PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> [3]. The main pathology mechanism of air pollution affecting the cardiovascular system includes systemic and local oxidative stress and inflammation that triggers endothelial dysfunction, platelet hyperreactivity and impaired vascular fibrinolytic function [4]. The local mechanism is caused by gases and soluble components of particulate matter, especially those with the smallest diameter which can easily cross the pulmonary epithelium and get into the blood stream. The systemic pathway is activated by pulmonary inflammation and oxidative stress, which was confirmed by the increasing level of pro inflammatory cytokines in the animal and human studies after short exposure to air pollutants [5]. Moreover, in experimental studies the autonomic imbalance favoring sympathetic activation leads to arrhythmia, vasoconstriction and hypertension [6].

All of these mechanisms may accelerate atherosclerosis, plaque instability and promote atherothrombosis, resulting in AMI and sudden death in short, as well as long-term observation. From an epidemiological point of view, the air pollutants are of important meaning as they can be qualified as modifiable risk factors of myocardial infarct and the prevention of air pollution should be included in national programs of cardiovascular disease prevention.

On the other hand, some non-modifiable factors have been considered to be triggering AMIs such as weather conditions [7]. Among meteorological variables, temperature [8] and barometric pressure [9] have been found to be prominently associated with MI.

Thus, it is of great importance to further investigate the influence of major air pollutants and meteorological variables which effect health status. The evaluation may be

especially valuable when performed in the most polluted areas where the scale of affect seems to have the strongest effect and may be more easily measured. It is also important to measure the effect in large enough and similar populations, based on serial observations that take into account not only polluted days but also refer to the periods of normal weather conditions.

Despite having a well-developed structure for optimal AMI treatment, Poland has been qualified as one of the European Union countries with highest rate of MI, stroke event rate and cardiovascular mortality. At the same time, Poland is one of the most air polluted countries in Europe, where fossil fuel is a major source of energy and the role of air pollution is underestimated [10]. This situation has prompted this study to perform an analysis that can evaluate the influences of all commonly measured air pollutants and weather condition parameters, separately on non-ST-segment elevation myocardial infarction (NSTEMI), ST-segment elevation myocardial infarction (STEMI) occurrence based on data selected from three typical, Polish, small and medium sized industrial cities.

## **METHODS**

### ***Database***

This study draws from a multicentre registry of acute myocardial infarctions of three AHP centers located in industrial cities in southern Poland: Kedzierzyn-Kozle (fifty-eight thousand inhabitants), Bielsko-Biala (one hundred seventy thousand inhabitants) and Mielec (sixty-two thousand inhabitants). Based on recently published registries these regions have qualified as some of the most air polluted regions in Europe [11]. Data collection covered a period from January 2014 to December 2015 from the regions of Bielsko-Biala, July 2014 to December 2015 from Kedzierzyn-Kozle and January 2015 to December 2015 from Mielec. The differences in these analyzed periods between centers are the result of different onset of air-quality monitoring in each city. All reported data come from local departments of interventional cardiology, which are the only centers providing 24/7 services in their regions. In the clinical data, both types of myocardial infarction admissions (STEMI and NSTEMI) were collected. The types of AMIs were established based on clinical data reported to the National Health Fund.

The air pollution and weather condition data for each city were collected as daily averages from a database audited by the Chief Inspectorate of Environmental Protection in

Poland. The following parameters were assembled: PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub>, barometric pressure, temperature and humidity. The cities were selected for this study based on the most complete and accurate data from air pollution measuring stations.

In order to present daily trends in particulate matter, concentrations over the analyzed period of time and were combined with the trends in the incidence of MI. The data was further divided into PM<sub>2.5</sub> and PM<sub>10</sub> consecutive thresholds in which each an increase in concentration of 10 µm/m<sup>3</sup> was translated into a higher threshold. In this division, the daily limit for PM<sub>2.5</sub> (25 µm/m<sup>3</sup>) was included in threshold 3 while the limit for PM<sub>10</sub> (50 µm/m<sup>3</sup>) was in threshold 6.

### *Statistical analysis*

The case-crossover design was used to explore the association between each type of AMI and air pollution exposure. In this type of analysis each case provides its own control, eliminating the influence of time-independent covariates, for instance hypertension, smoking, hypercholesterolemia and others. [12]. The value of each pollutant, barometric pressure, temperature and humidity during the day of MI occurrence or the previous day to MI were considered in each case. The median level of each of the above-mentioned variables from the 7 days prior to MI were taken as a control. The present study was focused on the short-term influence of each variable on NSTEMI or STEMI occurrence, and was restricted to the day of exposure (day 0) and the following day after exposure (day 1).

In statistical analysis, conditional logistic regression was used to assess the odds ratio (OR) with 95% confidence intervals (95% CI). Analysis was performed for a 10 µm/m<sup>3</sup> increase in air pollutants, 10°C increase in temperature, 10% increase in humidity and 10 mmHg change in the barometric pressure. The correlation between air pollutants and weather conditions were calculated using the Spearman correlation. P value ≤ 0.05 was considered as statistically significant.

## **RESULTS**

The air quality in all cities were comparable based on the latest World Health Organization (WHO) report [11] and measurements of air pollutants (Table 1). Full data on air pollution measurement were available for 89% (1462 days) over the observation time

period and 1957 cases of MI were analyzed. Precise characteristics of data collected are seen in Table 2. The reason for days missing was the lack of respective measurements of air quality due to periodic failures of local pollution measuring stations. If any measurement was missing during this period, it was excluded from study.

NSTEMI was presented during 686 days with complete, available pollution measurements and its total was 985 cases. STEMI was presented during 666 days with complete, available pollution measurements and the total number of cases was 972. Daily means of incidences in all centers were as follows: NSTEMI  $0.67 \pm 0.86$  cases, STEMI  $0.66 \pm 0.87$  cases and AMI's  $1.33 \pm 1.24$  cases. Detailed information about daily mean incidence occurrence was separate for all cities and are represented in Table 3.

The main descriptive statistics for variables are presented in Table 4. The correlations between variables are presented in Table 5. The highly positive correlations were observed between PM<sub>2.5</sub> and PM<sub>10</sub> ( $R = 0.9$ ) or PM<sub>10</sub> and NO<sub>2</sub> ( $R = 0.71$ ), respectively. The intermediate or negative correlations were for O<sub>3</sub> and humidity ( $R = -0.64$ ), SO<sub>2</sub> and temperature ( $R = -0.63$ ), O<sub>3</sub> and nitrogen oxides ( $R = -0.63$  for NO and  $-0.6$  for NO<sub>2</sub>).

### ***NSTEMI***

In the main analysis, both particulate matters including PM<sub>2.5</sub> and PM<sub>10</sub> had significant influence on NSTEMI occurrence on the day of air pollution exposure (OR = 1.099, CI 1.016–1.188,  $p = 0.018$  for PM<sub>2.5</sub> and OR = 1.078, CI 1.007–1.153,  $p = 0.03$  for PM<sub>10</sub>). Moreover, during the following day after air pollution, the exposure that triggered NSTEMI occurrence included SO<sub>2</sub> (OR = 1.522, CI 1.112–2.084,  $p = 0.009$ ) and both types of particulate matters: PM<sub>2.5</sub> (OR = 1.093, CI 1.011–1.181,  $p = 0.025$ ), PM<sub>10</sub> (OR = 1.077, CI 1.009–1.150,  $p = 0.025$ ). An extensive analysis for NSTEMI is presented in Figure 1.

### ***STEMI***

The most important triggers for STEMI occurrence on the day of air pollution were gaseous pollutants including SO<sub>2</sub> (OR = 1.670, CI 1.230–2.266,  $p = 0.001$ ), NO<sub>2</sub> (OR = 1.287, CI 1.061–1.562,  $p = 0.011$ ) and both particulate matters: PM<sub>2.5</sub> (OR = 1.197, CI 1.094–1.311,  $p < 0.001$ ) and PM<sub>10</sub> (OR = 1.163, CI 1.079–1.253,  $p < 0.001$ ). Similar results were seen on the following day after exposure and included SO<sub>2</sub> (OR = 1.550, CI 1.140–2.108,  $p = 0.005$ ), NO<sub>2</sub> (OR = 1.265, CI 1.041–1.538,  $p = 0.018$ ), PM<sub>2.5</sub> (OR = 1.172, CI

1.076–1.276,  $p < 0.001$ ) and PM10 (OR = 1.131, CI 1.053–1.215,  $p < 0.001$ ). Detailed results for STEMI are presented in the Figure 2.

None of the weather conditions including temperature, barometric pressure and humidity reached statistical significance regarding to both types of MI and time periods.

## **DISCUSSION**

According to the latest WHO report, Poland is the most air-polluted region among European Union countries [11]. At the beginning of 2017, measured concentrations of PM2.5 and PM10 in some regions of Poland reached over 30 times recommended limits. The values had never been observed thus far in past years. Interestingly, this deterioration in air quality coincided with almost , fourteen thousand additional deaths in Poland compared to demographic data from January to February years 2016 and 2017 (Table 6, Based on Polish Central Statistical Office data) [13].

Confirmation of this serious situation in selected Polish cities are recorded in maximum values of air pollutants in Table 1, where the guideline limits are exceeded by up to 1000%. What is more, analyzing Table 3, during tested period about 35% of these days were above the daily limit of PM2.5. In addition, there is a lack of sufficient governmental action over the last decades to limit gas and dust emissions, leading to systematic worsening of air pollution in Poland.

In the currently available literature, there remains a lack of studies examining the role of air pollution on myocardial infarction occurrence in such polluted regions. In addition, only a few worldwide studies which have evaluated the influence of air pollution separately on NSTEMI and STEMI events. Most of the analyses were focused only on the impact of the particulate matters and overlooked the weather influence and gaseous pollutants. The present study takes into consideration a large number of air pollutants and weather conditions including: temperature, barometric pressure and humidity. It is also important to evaluate the influence of air pollution on AMI occurrence in the setting of a local environment. These features, as well as the number of variables and data taken into analysis from three different centers and cities make this study precise and plausible.



The present study found differences in the level of air pollution and its influence on each type of MI occurrence. These results have presented that the STEMI events are especially associated with particulate matters: PM<sub>10</sub>, PM<sub>2.5</sub> and gaseous pollutants: SO<sub>2</sub> and NO<sub>2</sub>. From particulate matters, the PM<sub>2.5</sub> played the main role, which concurs with findings reported by other researchers [14]. Similar effects were seen during both examining days, which provides evidence that air pollution essentially has an impact on STEMI events. Comparable results of air pollution influence on STEMI occurrence were reported by other studies. Argacha et al. [15] found an association between STEMI and both particulate matters and NO<sub>2</sub>, which had the most significant impact, but SO<sub>2</sub> was not included in this study. Pope et al. [16] in a large study, also found a similar association between STEMI and PM<sub>2.5</sub> which was the only pollutant evaluated in the analysis.

On the other hand, weaker relationships were seen between air pollution and NSTEMI occurrence. Only particulate matter turn out to be statistically significant during the day of exposure to air pollution. The day after exposure, the importance in triggering NSTEMI had been reached by: PM<sub>10</sub>, PM<sub>2.5</sub> and SO<sub>2</sub>. In the literature there are only a few studies showing evidence of air pollution influence on NSTEMI occurrence. This can be caused by the especially small number of studies exploring both types of AMI separately. Only the association between NSTEMI and daily maximum 1-h level of NO<sub>2</sub> was confirmed by Butland et al. [17], but in this study the SO<sub>2</sub> was not evaluated. Present findings regarding NSTEMI may also be caused by the high level of air pollution in Poland, which can exert significant influence on its appearance.

What is more, current results observed higher values of odds ratios for each 10  $\mu\text{m}^3$  increase in gaseous pollutants than particulate matters. This can be explained by a lower spread of its minimal and maximal levels, compared to other pollutants, mainly PM's. These findings confirm, that not only particulate matters play role in triggering MI, but the most dangerous for human health is a combination of gaseous pollutants, especially SO<sub>2</sub> and NO<sub>2</sub> with particulate matters, above PM<sub>2.5</sub>.

To summarize, the results of the current study clearly show that air pollution should be regarded as one of the modifiable risk factors of cardiovascular diseases that are the main cause of mortality in western countries and contribute to a serious economic burden with substantial loss of productivity and GDP value. Only coordinated governmental and local actions focused on air quality improvement in combination with an increase in health care

expenditures may significantly improve the quality of life for patients, reduce total mortality rate, and positively influence the economy. Unfortunately, in many countries the problem remains underestimated causing a serious health threat. For instance, despite the fact that Poland is the most air-polluted region among European Union countries, the government instead of setting a priority for making air cleaner has recently and dangerously reduced expenditures on cardiology and the development of green energy production, putting patients at serious risk of increased mortality and morbidity.

### ***Limitations of the study***

The current study has some limitations. In a case-crossover design, the choice of a control period is crucial for results. A median value was taken of each variable for seven days preceding MI occurrence. It seems to be the most neutral value, which can present the short-term changes in air quality and weather conditions. The study also has the same weakness, such as a lack of carbon monoxide levels, which theoretically can also impact MI occurrence.

## **CONCLUSIONS**

The most important pollutants triggering STEMI and NSTEMI occurrence in 3 populations of southern Poland, both on the day of air pollution and the following day are particular PM<sub>2.5</sub> and PM<sub>10</sub> matter and gaseous pollutants including NO<sub>2</sub> and SO<sub>2</sub>. These pollutants should be regarded as modifiable risk factors and thus their reduction is a priority in order to decrease total morbidity and mortality.

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**Table 1.** Air quality in selected cities [11].

Center	Days above PM2.5 (25 µm/m <sup>3</sup> ) limit (% of tested period)	Annual mean of PM2.5	Days above PM10 (50 µm/m <sup>3</sup> ) limit (% of tested period)	Annual mean of PM10	Place in WHO report
Bielsko-Biala	233 days (34%)	34 µm/m <sup>3</sup>	142 days (21%)	41 µm/m <sup>3</sup>	32
Kedzierzyn-Kozle	187 days (43%)	33 µm/m <sup>3</sup>	80 days (18.5%)	39 µm/m <sup>3</sup>	37

Mielec	132 days (38%)	31 $\mu\text{m}/\text{m}^3$	61 days (18%)	42 $\mu\text{m}/\text{m}^3$	56
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WHO — World Health Organization

**Table 2.** Main characteristic of data collected from different centers.

Center	Period	Available data (%)	MI cases	NSTEMI cases	STEMI cases
All centers	1644 days	1462 days (89%)	1957	985	972
Bielsko-Biala	2014–2015 (730 days)	682 days (93%)	1185	561	624
Kedzierzyn-Kozle	July 2014–2015 (549 days)	433 days (79%)	443	252	191
Mielec	2015 (365 days)	347 days (95%)	329	172	157

MI — myocardial infarction; NSTEMI — non-ST-segment elevation myocardial infarction; STEMI — ST-segment elevation myocardial infarction

**Table 3.** Mean daily occurrence of acute myocardial infarction.

Center	MI daily	NSTEMI daily)	STEMI daily
All centers	1.33 $\pm$ 1.24	0.67 $\pm$ 0.86	0.66 $\pm$ 0.87
Bielsko-Biala	1.73 $\pm$ 1.35	0.82 $\pm$ 0.95	0.91 $\pm$ 0.99
Kedzierzyn-Kozle	1.02 $\pm$ 1.03	0.58 $\pm$ 0.77	0.44 $\pm$ 0.68
Mielec	0.95 $\pm$ 1.02	0.49 $\pm$ 0.74	0.45 $\pm$ 0.70

Data are shown as mean  $\pm$  standard deviation. MI — myocardial infarction; NSTEMI — non-ST-segment elevation myocardial infarction; STEMI — ST-segment elevation myocardial infarction

**Table 4.** Descriptive statistics for each variable measured.

Variable	Median	Minimum	Maximum	Mean	$\pm$ SD
PM2.5 [ $\mu\text{m}/\text{m}^3$ ]	20	3	256	27.59	22.89
PM10 [ $\mu\text{m}/\text{m}^3$ ]	27	5	260	35.41	26.26
SO2 [ $\mu\text{m}/\text{m}^3$ ]	5	0.7	80	7.56	6.63

NO2 [ $\mu\text{m}/\text{m}^3$ ]	16	3	69	17.80	8.55
O3 [ $\mu\text{m}/\text{m}^3$ ]	51	1	127	50.26	23.84
Barometric pressure [hPa]	987	932	1021	984.04	15.36
Temperature [ $^{\circ}\text{C}$ ]	9	-18	29	9.64	8.06
Humidity [%]	78	31	99	77.25	14.21

PM2.5 — particulate matter with diameter < 2.5  $\mu\text{m}$ ; PM10 — particulate matter with diameter < 10  $\mu\text{m}$ ; SO2 — sulfur dioxide; NO2 — nitrogen dioxide; O3 — ozone; SD — standard deviation

**Table 5.** Spearman correlations between variables. All statistically significant correlations are highlighted.

Variable	Pm 10	PM2.5	SO2	No2	O3	Barometric pressure	Temperature	Humidity
PM10	1.00	0.90	0.64	0.71	-0.47	0.21	-0.40	0.09
PM2.5	0.90	1.00	0.61	0.65	-0.51	0.21	-0.43	0.16
SO2	0.64	0.61	1.00	0.59	-0.41	-0.10	-0.63	0.19
NO2	0.71	0.65	0.59	1.00	-0.60	-0.02	-0.38	0.32
O3	-0.47	-0.51	-0.41	-0.60	1.00	-0.18	0.56	-0.64
Barometric pressure	0.21	0.21	-0.10	-0.02	-0.18	1.00	0.12	-0.34
Temperature	-0.40	-0.43	-0.63	-0.38	0.56	0.12	1.00	-0.49
Humidity	0.09	0.16	0.19	0.32	-0.64	-0.34	-0.49	1.00

PM2.5 — particulate matter with diameter < 2.5  $\mu\text{m}$ ; PM10 — particulate matter with diameter < 10  $\mu\text{m}$ ; SO2 — sulfur dioxide; NO2 — nitrogen dioxide; O3 — ozone

**Table 6.** Differences in Polish population statistics [13].

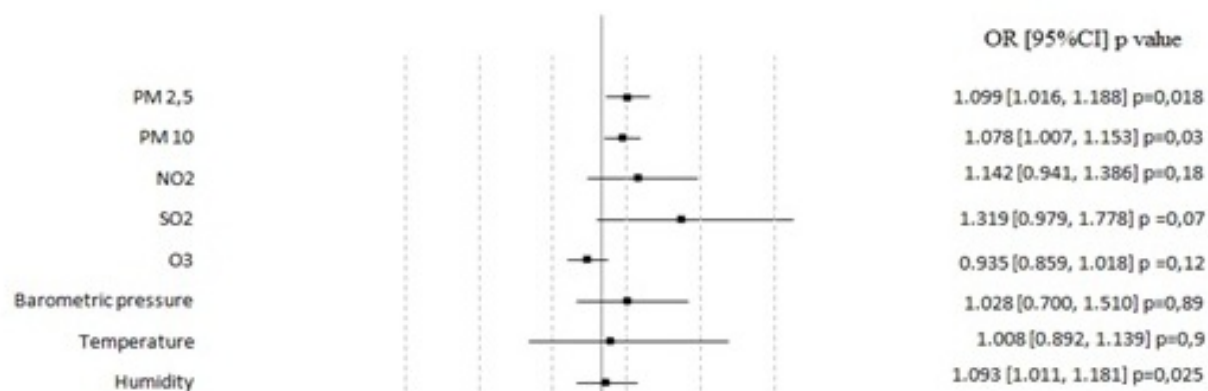
Month	2016	2017	Change in amount (%)
January	33,000	44,400	+11,400 (+35%)
February	34,900	37,400	+2,500 (+7%)
Total	67,900	81,800	+13,900 (+20.5%)

## FIGURE LEGENDS

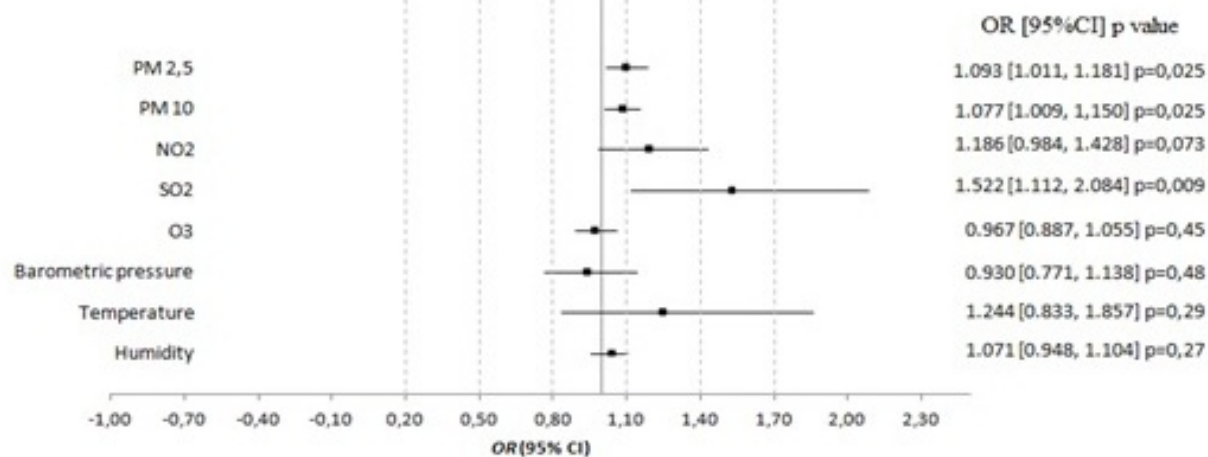
**Figure 1.** Logistic regression model for non-ST-segment elevation myocardial infarction (NSTEMI) occurrence; PM 2.5 — particulate matter with diameter < 2.5  $\mu\text{m}$ ; PM10 — particulate matter with diameter < 10  $\mu\text{m}$ ; SO<sub>2</sub> — sulfur dioxide; NO<sub>2</sub> — nitrogen dioxide; O<sub>3</sub> — ozone; OR — odds ratio; CI — confidence interval.

**Figure 2.** Logistic regression model for ST-segment elevation myocardial infarction (STEMI) occurrence; PM 2.5 — particulate matter with diameter < 2.5  $\mu\text{m}$ ; PM10 — particulate matter with diameter < 10  $\mu\text{m}$ ; SO<sub>2</sub> — sulfur dioxide; NO<sub>2</sub> — nitrogen dioxide; O<sub>3</sub> — ozone; OR — odds ratio; CI — confidence interval.

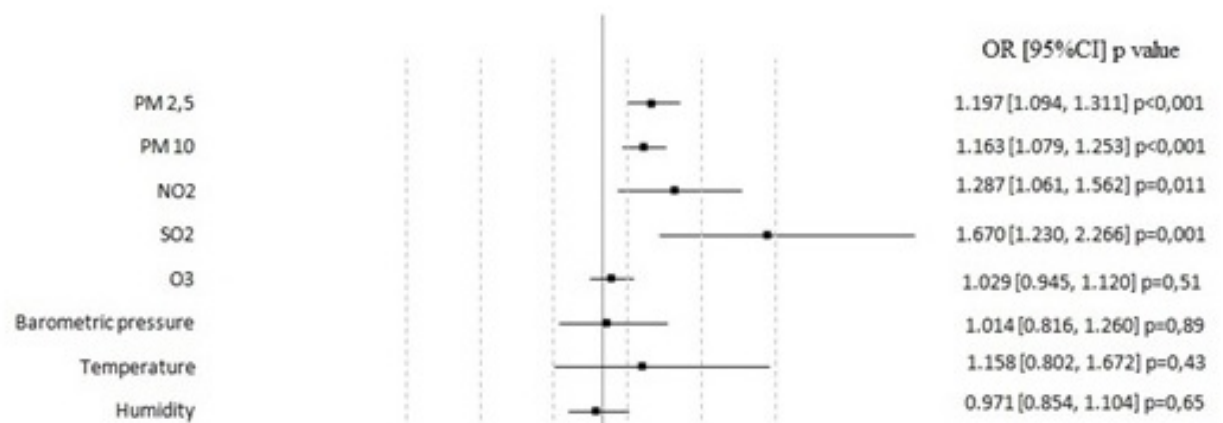
DAY 0



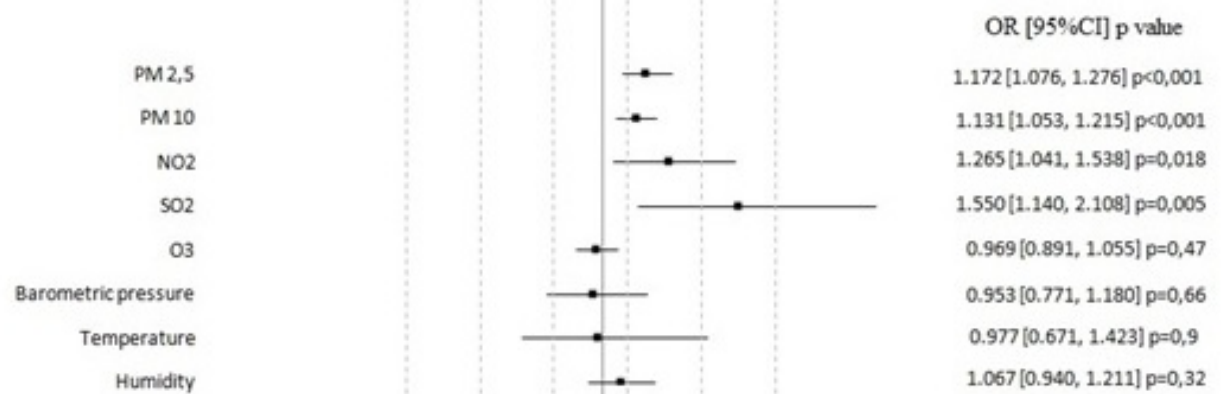
DAY 1



DAY 0



DAY 1



-1,00 -0,70 -0,40 -0,10 0,20 0,50 0,80 1,10 1,40 1,70 2,00 2,30  
OR (95% CI)