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Short-term exposure to particulate matters is associated with septic emboli in infective endocarditis

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Abstract

This survey was to investigate the short-term effect of particulate matters (PMs) exposure on clinical and microbiological variables, especially septic emboli, in infective endocarditis (IE). The study analyzed 138 IE patients in Far Eastern Memorial Hospital from 2005 to 2015 and clinical variables were retrospectively requested. The data of air quality were recorded and collected by a network of 26 monitoring stations spreading in Northern part of Taiwan. We found that IE patients with septic emboli were found to be exposed to a significantly higher level of PM2.5 (32.01 ± 15.89 vs. $21.70 \pm 13.05 \mu g/m^3$, $P < .001$) and PM10 (54.57 ± 24.43 vs $40.98 \pm 24.81 \mu g/m^3$, $P = .002$) on lag 0 day when compared to those without. Furthermore, multivariate regression analysis revealed that that ambient exposure to PM2.5 (odds ratio: 3.87, 95% confidence interval: 1.31–8.31; $P = .001$) and PM10 (odds ratio: 4.58, 95% confidence interval: 2.03–10.32; $P < .001$) significantly increased risk of septic emboli in IE patients. To our knowledge, this is the first study demonstrating that short-term exposure to PMs was associated with septic emboli in IE.

Abbreviations: CI = confidence interval, ICD = international classification diseases, IE = infective endocarditis, IL = interleukin, IQR = interquartile ranges, MRSA = methicillin-resistant Staphylococcus aureus, OHCA = out-of-hospital cardiac arrest, OR = odds ratio, PM = particulate matter, ROC = receiver operating characteristic, TLR = toll-like receptor, TNF = tumor necrosis factor.

Keywords: infective endocarditis, particulate matter 10, particulate matter 2.5, septic emboli

1. Introduction

Accumulating evidence has revealed that exposure to ambient particulate matter (PM2.5 and PM10) was associated with numerous cardiovascular (e.g., ischemic heart diseases, heart failure, cerebrovascular diseases) and pulmonary diseases (e.g., chronic obstructive pulmonary diseases, respiratory tract infection, lung cancer).[1,2] Recently, PM2.5 exposure was found to

contribute to the occurrence and adverse outcomes of other non-cardiopulmonary diseases, including out-of-hospital cardiac arrest (OHCA),[3–5] Parkinson disease,[6] ischemic stroke,[7] liver-[8] and kidney-related diseases,[9,10] cancer,[11,12] and so on. However, the relationship between exposure to air pollutants and infective endocarditis (IE) remains to be explored.

The infection in the endocardium with vegetation or intracardiac abscess, namely IE, is relatively rare but could be life-threatening with high mortality rate of 9% to 30%.[13] IE could also be accompanied with a broad spectrum of systemic complications because of septic emboli, leading to localized thrombosis, metastatic infection and systemic immune reaction. It was reported that approximately 12% to 40% of IE patients experienced embolic events.[13] Besides, several risk factors were identified for IE, including cardiac (valvular heart disease,[14] replacement of prosthetic heart valve, previous IE history[15]) and non-cardiac (intravenous drug use,[16,17] dental infection,[18,19] hemodialysis[20,21] or peritoneal dialysis[22]). Nevertheless, the association of air pollutants with septic emboli, other risk factors in clinical and microbial species in IE patients remains unknown.

Therefore, we aimed to investigate the effect of PM2.5 and PM10 exposure on clinical and microbiological variables in IE patients. We also investigated whether septic emboli were associated with clinical and microbiological features as well as PM2.5 and PM10 exposure in IE patients.

2. Experimental section

2.1. Study design and patient population

From May 1st, 2005 to December 31st, 2015, patients visiting the outpatient department or emergency department in Far Eastern Memorial Hospital with international classification diseases,

9th edition (ICD-9) code of 421.0, 421.1, 421.9, 424.90, 424.91, or 424.99 were retrospectively reviewed. Those who had blood cultures collected on the visiting day and met the modified Duke criteria for definite and possible IE were enrolled. Clinical data including age, gender, predisposing clinical factors (prior history of IE, valvular heart disease or placement of prosthetic valve, intravenous drug use, hemodialysis or peritoneal dialysis, dental infections), microbiological results of blood culture, surgical intervention or antibiotic treatment and length of hospital stay were collected via reviewing the electronic medical record. The report of cardiac echography (by transthoracic or transesophageal echography) was acquired and the heart valve location of vegetation or lesion was recorded. Besides, the presence of septic emboli was considered with completion of imaging study and verified by the radiologist. The residential district in individuals was also collected. The research approval was acquired from the research ethics committee of FEMH (106130-E) and the investigation was conducted in accordance with the *Declaration of Helsinki* in 1964.

2.2. Data collection and analysis for PM2.5 and PM10

The report of air quality status in Taiwan from May 1st, 2005 to December 31st, 2015 was referred to the Taiwan Air Quality Monitoring Network manipulated by the Environmental Protection Administration. The data of air quality were recorded by a network of 26 monitoring stations spreading in Northern part of Taiwan (Taipei city, New Taipei city and Taoyuan city). The parameters of air quality, PM2.5 and PM10, recorded by the nearest monitoring station to patients' residential district were collected. The 24-hour mean concentration of PM2.5 and PM10 on the visiting day (lag 0 day), as well as the lag 1 and lag 2 day of each patient were acquired for analysis of the short-term effect of air pollutant exposure on clinical and microbiological features in IE patients.

2.3. Statistical analysis

Statistical analyses were performed using the SPSS (version 19.0; SPSS Inc., Chicago, IL) statistical software for data analysis. The descriptive data were expressed as the mean ± standard deviation or median with interquartile ranges (IQR). For categorical data, Pearson's chi-squared test or Fisher exact test was performed; and for continuous data, the student's *t* test was applied for statistical analyses. The optical cut-off values were determined by receiver operating characteristic (ROC) analysis with a high Youden index value. Besides, univariate analysis for clinical and microbiological features as well as parameters of air quality was performed. The above factors with the p value of 0.10 and less would be further adjusted in the multivariate binary logistic regression models. The data was presented with odds ratio (OR) with 95% confidence interval (CI). Statistical significance was considered if the P value was less than .05.

3. Results

During the study interval, a total of 295 patients with ICD-9 code of 421.0, 421.1, 421.9, 424.90, 424.91, or 424.99 were retrospectively reviewed; and 138 who met the modified Duke criteria for definite and possible IE were enrolled. The demographic data of the study population were shown in Table 1. In microbiological distribution in these IE patients

Table 1

The demographic data in patients with infectious endocarditis.

Variables	Values
Age (yr)	54 (36–66)
Gender (male/female)	93/45
Predisposition	97 (70.3%)
Intravenous drug use	38 (27.5%)
Prior placement of prosthetic valve	26 (18.8%)
Prior valvular heart disease	25 (16.9%)
Hemodialysis/peritoneal dialysis	19 (13.8%)
Prior history of infectious endocarditis	17 (12.3%)
Dental infections	9 (6.5%)
Diagnosis by modified Duke criteria	
Definitive	109 (79.0%)
Possible	29 (21.0%)
Lesion location	
Left-sided	
Aortic valve	32 (23.2%)
Mitral valve	62 (44.9%)
Aortic valve plus mitral valve	5 (3.6%)
Right-sided	
Tricuspid valve	27 (19.6%)
Pulmonary valve	1 (0.7%)
Both-sided	
Aortic valve plus tricuspid valve	3 (2.2%)
Mitral valve plus tricuspid valve	2 (1.4%)
Not found	6 (4.3%)
Septic embolization	60 (43.5%)
Central nervous system	22 (15.9%)
Lung	15 (10.9%)
Spleen	9 (6.5%)
Kidney	6 (4.3%)
Extremities	6 (4.3%)
Liver	4 (2.9%)
Bone and joint structures	3 (2.2%)
Coronary vessels	1 (0.7%)
Management	
Antibiotic treatment only	71 (51.4%)
Surgical intervention plus antibiotic treatment	67 (48.6%)
Length of hospital stay (days)	29 (19–38)

Data were expressed in median with interquartile range or number (percentage).

(Table 2), Staphylococci infection (n=59, 42.8%) was the most common, followed by Streptococci (n=35, 25.4%), Enterococci (n=9, 6.5%) and Candida infections (n=3, 2.2%). Of IE patients with Staphylococci infection, 21 were infected by methicillin-resistant Staphylococcus aureus (MRSA). Besides, other species of microorganism, including *Abiotrophia defectiva, Aggregatibacter aphrophilus, Arcanobacterium haemolyticum, Bacillus species, Bacteroides fragilis, Campylobacter, Haemophilus parainfluenza, Klebsiella pneumoniae, Pasteurella* like organism, *Proteus mirabilis, Pseudomonas aeruginosa, Ralstonia pickettii, Rhodococcus species,* and *Serratia marcescens,* were yielded in blood culture in IE. There was negative finding in blood culture of 14 IE patients.

As shown in Table 3, the association of PM2.5 and PM10 exposure with the clinical and microbiological features in IE patients was further investigated. The patients were divided into 2 groups with and without the specified factors; and the exposed levels of PM2.5 and PM10 on lag 0 day, and mean PM2.5 and PM10 from lag 0 to lag 2 days were compared in the two groups. The results revealed that the exposed concentrations of PM2.5 on lag 0 day (32.01 ± 15.89 vs $21.70 \pm 13.05\ \mu g/m^3$, $P < .001$), mean

Table 2

The microbiological distribution in patients with infectious endocarditis.

Organisms	Total (n=138)	Right-sided (n=28)	Left-sided (n=99)	Both-sided (n=5)
Staphylococci	59	24	30	2
MSSA	38	16	19	1
MRSA	21	8	11	1
Streptococci	35	2	31	1
Enterococci	9	–	7	1
Abiotrophia defectiva	1	–	1	–
Aggregatibacter aphrophilus	2	–	2	–
Arcanobacterium haemolyticum	1	–	1	–
Bacillus species	1	–	1	–
Bacteroides fragilis	1	–	1	–
Campylobacter	1	–	1	–
Candida species	3	–	3	–
Haemophilus parainfluenza	2	–	2	–
Klebsiella pneumoniae	2	–	2	–
Pasteurella like organism	1	–	1	–
Proteus mirabilis	1	–	1	–
Pseudomonas aeruginosa	1	–	1	–
Ralstonia pickettii	2	–	2	–
Rhodococcus species	1	1	–	–
Serratia marcescens*	1	–	1	–
No growth	14	1	12	1

MRSA = methicillin-resistant Staphylococcus aureus, MSSA = methicillin-sensitive Staphylococcus aureus.

* Serratia marcescens was found accompanied with beta-Streptococcus group.

PM2.5 from lag 0 to lag 2 days (30.68 ± 12.99 vs $23.18 \pm 11.19\,\mu g/m^3$, $P < .001$), PM10 on lag 0 day (54.57 ± 24.43 vs $40.98 \pm 24.81\,\mu g/m^3$, $P = .002$) and mean PM10 from lag 0 to lag 2 days (51.92 ± 18.77 vs $42.27 \pm 19.70\,\mu g/m^3$, $P = .004$) were significantly higher in the group with septic emboli when compared to the group without. Besides, the exposed concentrations of PM10 on lag 0 day (54.57 ± 24.43 vs $40.98 \pm 24.81\,\mu g/m^3$, $P = .010$) and mean PM10 from lag 0 to lag 2 days (51.92 ± 18.77 vs $42.27 \pm 19.70\,\mu g/m^3$, $P = .039$) were significantly higher in the group with positive findings in blood culture in comparison with the group without. It was also revealed that the exposed concentrations of PM10 on lag 0 day (54.57 ± 24.43 vs $40.98 \pm 24.81\,\mu g/m^3$, $P = .024$) and mean PM10 from lag 0 to lag 2 days (51.92 ± 18.77 vs $42.27 \pm 19.70\,\mu g/m^3$, $P = .013$) were significantly higher in the group with infection by other microorganisms except Staphylococci, Streptococci, and Enterococci when compared to the group without. There was no statistical difference between groups with and without other specified factors.

Since we found that exposed concentration of air pollutants was significantly higher in IE patients with septic emboli than those without, we further performed univariate analysis to find out if there were any confounding factors. As shown in Table 4, definite IE diagnosed by the modified Duke criteria (OR: 2.97, 95% CI: 1.17–7.54; $P = .018$), positive findings in blood culture (OR: 5.27, 95% CI: 1.13–24.55; $P = .023$), PM2.5 of $25\,\mu g/m^3$ and more on lag 0 day (OR: 3.89, 95% CI: 1.91–7.92; $P < .001$) and PM10 of $50\,\mu g/m^3$ and more on lag 0 day (OR: 3.55, 95% CI: 1.72–7.32; $P = .001$) were significantly associated with septic

Table 3

The clinical and microbiological features of patients with infectious endocarditis exposed to PM2.5 and PM10 concentrations.

Variables	PM2.5 (lag 0) With	PM2.5 (lag 0) Without	PM2.5 (lag 0 to lag 2) With	PM2.5 (lag 0 to lag 2) Without	PM10 (lag 0) With	PM10 (lag 0) Without	PM10 (lag 0 to lag 2) With	PM10 (lag 0 to lag 2) Without
Age > 65 years	26.57 ± 18.49	26.03 ± 13.78	26.26 ± 15.85	26.51 ± 11.04	49.72 ± 30.66	45.78 ± 23.20	46.96 ± 22.95	46.27 ± 18.57
Female gender	27.86 ± 16.41	25.37 ± 14.58	27.34 ± 13.82	26.01 ± 11.91	50.24 ± 28.43	45.27 ± 23.90	47.79 ± 21.53	45.82 ± 19.03
Intravenous drug use	25.10 ± 11.50	26.59 ± 16.41	26.21 ± 9.47	26.53 ± 13.55	44.11 ± 18.61	47.94 ± 27.65	45.17 ± 14.24	46.96 ± 21.61
Prosthetic valve placement	24.01 ± 17.92	26.68 ± 14.53	24.39 ± 10.99	26.92 ± 12.86	42.37 ± 26.52	47.94 ± 25.23	42.04 ± 16.67	47.49 ± 20.41
Prior valvular heart disease	26.55 ± 16.35	24.82 ± 12.16	26.50 ± 13.38	26.30 ± 10.37	48.24 ± 27.61	43.69 ± 19.45	47.02 ± 21.51	45.14 ± 15.25
HD/PD	26.36 ± 8.95	26.15 ± 15.99	27.59 ± 10.55	26.26 ± 12.84	49.55 ± 19.86	46.47 ± 26.30	49.53 ± 20.11	45.98 ± 19.82
Prior IE history	29.50 ± 20.65	25.71 ± 14.31	28.81 ± 13.71	26.11 ± 12.38	49.58 ± 31.36	46.51 ± 24.67	47.78 ± 21.73	46.28 ± 19.63
Definitive IE	26.84 ± 15.25	23.68 ± 14.94	26.75 ± 12.29	25.29 ± 13.54	47.32 ± 25.31	45.27 ± 26.47	47.01 ± 20.25	44.42 ± 18.31
Lesion location at left side	26.29 ± 15.64	27.51 ± 14.60	26.27 ± 12.50	28.34 ± 13.59	47.32 ± 27.00	47.40 ± 23.20	46.87 ± 21.26	46.82 ± 17.13
Septic embolization	32.01 ± 15.89***	21.70 ± 13.05	30.68 ± 12.99***	23.18 ± 11.19	54.57 ± 24.43**	40.98 ± 24.81	51.92 ± 18.77**	42.27 ± 19.70
Surgical intervention	26.72 ± 15.62	25.70 ± 14.89	27.02 ± 13.47	25.92 ± 11.70	48.22 ± 26.28	45.70 ± 24.86	47.97 ± 22.02	45.12 ± 17.68
LHS > 28 days	27.05 ± 16.11	25.26 ± 14.22	27.48 ± 12.99	25.34 ± 12.02	48.38 ± 26.42	45.31 ± 24.53	47.73 ± 20.64	45.13 ± 18.98

Organisms	PM2.5 (lag 0) With	PM2.5 (lag 0) Without	PM2.5 (lag 0 to lag 2) With	PM2.5 (lag 0 to lag 2) Without	PM10 (lag 0) With	PM10 (lag 0) Without	PM10 (lag 0 to lag 2) With	PM10 (lag 0 to lag 2) Without
Positive findings	26.72 ± 15.53	21.41 ± 11.09	26.71 ± 12.74	24.03 ± 10.60	48.15 ± 26.20**	35.74 ± 13.98	47.26 ± 20.44*	39.46 ± 11.43
Staphylococci	24.96 ± 13.47	27.09 ± 16.38	26.06 ± 11.87	26.72 ± 13.07	44.64 ± 22.54	48.57 ± 27.48	45.05 ± 17.88	47.53 ± 21.21
MSSA	22.95 ± 11.64	27.41 ± 16.22	24.03 ± 9.69	27.36 ± 13.38	42.47 ± 20.40	48.57 ± 27.06	43.10 ± 16.21	47.74 ± 20.97
MRSA	28.61 ± 15.92	25.74 ± 15.08	29.74 ± 14.58	25.85 ± 12.10	48.56 ± 26.03	46.59 ± 25.47	48.56 ± 20.53	46.09 ± 19.76
Streptococci	25.78 ± 17.14	26.32 ± 14.53	25.60 ± 14.24	26.74 ± 11.93	44.51 ± 25.77	47.73 ± 25.44	44.74 ± 21.69	47.07 ± 19.20
Enterococci	28.43 ± 15.82	26.02 ± 15.20	25.18 ± 12.81	26.53 ± 12.55	51.55 ± 18.80	46.56 ± 25.90	44.45 ± 13.47	46.61 ± 20.22
Others	32.82 ± 17.57	25.05 ± 14.53	31.34 ± 12.25	25.61 ± 12.43	63.53 ± 34.67*	44.07 ± 22.57	59.56 ± 24.38*	44.24 ± 18.15

The unit of PM2.5 and PM10 is $\mu g/m^3$.

IE = infectious endocarditis, HD = hemodialysis, PD = peritoneal dialysis, LHS = length of hospital stay, MSSA = methicillin-sensitive Staphylococcus aureus, MRSA = methicillin-resistant Staphylococcus aureus.

* $P < .05$, ** $P < .01$, *** $P < .001$, when compared with group without the risk factor.

Table 4

The association of clinical and microbiological features and fine particulate matter with septic emboli in patients with infectious endocarditis.

Variables	Univariate analysis		Multivariate analysis with the model adjusted by PM2.5 (lag 0)		Multivariate analysis with the model adjusted by PM10 (lag 0)	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age > 65 years	0.40 (0.18–0.89)	.023	0.47 (0.19–1.16)	.102	0.38 (0.15–0.96)	.042
Female gender	0.94 (0.46–1.93)	.873	0.85 (0.36–2.00)	.711	0.75 (0.32–1.74)	.502
Intravenous drug use	1.67 (0.79–3.54)	.181	NA	NA	NA	NA
Prosthetic valve placement	0.41 (0.16–1.05)	.059	0.54 (0.19–1.49)	.233	0.49 (0.17–1.39)	.181
Prior valvular heart disease	0.85 (0.41–1.77)	.659	NA	NA	NA	NA
HD/PD	1.20 (0.45–3.17)	.713	NA	NA	NA	NA
Prior IE history	0.68 (0.24–1.95)	.467	NA	NA	NA	NA
Definitive IE	2.97 (1.17–7.54)	.018	2.12 (0.76–5.93)	.150	2.40 (0.84–6.83)	.101
Lesion location at left side	0.97 (0.44–2.11)	.931	NA	NA	NA	NA
Surgical intervention	1.11 (0.57–2.17)	.765	NA	NA	NA	NA
LHS > 28 days	0.90 (0.46–1.77)	.765	NA	NA	NA	NA
Microbiological results of blood culture	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Staphylococci	1.91 (0.96–3.79)	.063	1.81 (0.81–4.03)	.147	1.99 (0.88–4.47)	.098
MSSA	1.24 (0.59–2.63)	.572	NA	NA	NA	NA
MRSA	2.42 (0.93–6.29)	.064	2.15 (0.74–6.29)	.161	1.97 (0.68–5.72)	.211
Streptococci	0.77 (0.36–1.68)	.517	NA	NA	NA	NA
Enterococci	0.63 (0.15–2.64)	.731	NA	NA	NA	NA
Others	1.36 (0.53–3.52)	.527	NA	NA	NA	NA
Positive findings	5.27 (1.13–24.55)	.023	4.46 (0.61–32.69)	.141	4.13 (0.55–31.06)	.169
Exposure to fine particulate matter	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
PM2.5 (lag 0) > 25 μg/m³	3.89 (1.91–7.92)	<.001	3.87 (1.81–8.31)	.001	NA	NA
PM10 (lag 0) > 50 μg/m³	3.55 (1.72–7.32)	.001	NA	NA	4.58 (2.03–10.32)	<.001

CI = confidence interval, HD = hemodialysis, IE = infectious endocarditis, LHS = length of hospital stay, MRSA = methicillin-resistant Staphylococcus aureus, MSSA = methicillin-sensitive Staphylococcus aureus, NA = not assessed, OR = odds ratio, PD = peritoneal dialysis.

emboli in IE patients. Besides, Staphylococci (OR: 1.91, 95% CI: 0.96–3.79; $P=.063$) and MRSA infections (OR: 2.42, 95% CI: 0.93–6.29; $P=.064$) were seemingly associated with septic emboli in IE patients. In contrast, age of 65 years and more (OR: 0.40, 95% CI: 0.18–0.89; $P=.023$) was significantly reversely associated with septic emboli in IE patients; and prior placement of prosthetic valve (OR: 0.41, 95% CI: 0.16–1.05; $P=.059$) was seemingly reversely associated with septic emboli in IE patients. The multivariate binary logistic regression analyses were then performed by 2 separate models with adjustment of PM2.5 and PM10 accompanied with adjustment of the above variables. In the model adjusted by PM2.5 and the above variables, PM2.5 of 25 μg/m³ and more on lag 0 day (OR: 3.87, 95% CI: 1.31–8.31; $P=.001$) was significantly associated with septic emboli in IE patients. We also performed the model adjusted by PM10 and the above variables, which showed that PM10 of 50 μg/m³ and more on lag 0 day (OR: 4.58, 95% CI: 2.03–10.32; $P<.001$) was significantly associated with septic emboli; and age of 65 years and more (OR: 0.38, 95% CI: 0.15–0.96; $P=.042$) was significantly reversely associated with septic emboli in IE patients.

Besides, considering that intravenous drug use (27.5%) may be more closely related to PM2.5 and PM10, we then excluded 38 patients with intravenous drug use for subgroup analysis. It was found that the exposed concentration of PMs remains significantly higher in the group with septic emboli when compared with those without. We also further performed univariate analysis and the results showed that definite IE diagnosed by the modified Duke criteria (OR: 3.50, 95% CI: 1.19–10.31,

$P=.018$), PM2.5 of 25 μg/m³ and more on lag 0 day (OR: 2.92, 95% CI: 1.27–6.70, $P=.010$) and PM10 of 50 μg/m³ and more on lag 0 day (OR: 3.09, 95% CI: 1.34–7.15, $P=.007$) were significantly associated with septic emboli in IE patients. Multivariate binary logistic regression analyses were further performed with confounding factors of age, gender and definite IE. In the model adjusted by PM2.5 and the above variables, PM2.5 of 25 μg/m³ and more on lag 0 day (OR: 2.75, 95% CI: 1.15–6.55; $P=.023$) was significantly associated with septic emboli in IE patients. Additionally, in the model adjusted by PM10 and the above variables, PM10 of 50 μg/m³ and more on lag 0 day (OR: 3.20, 95% CI: 1.32–7.77; $P=.010$) was significantly associated with septic emboli in IE patients. Compared with the original results including IE patients with IV drug abuse and the non-including group, it was shown that exposure to PMs remained an association with septic emboli in IE. The above results suggested that exposure to PM2.5 and PM 10 could be a critical factor for contribution to septic emboli in IE patients.

4. Discussion

Our main findings indicated that in IE patients with septic emboli and positive findings in blood culture, especially in which the species except Staphylococci, Streptococci and Enterococci were yielded, were found to be exposed to a significantly higher level of PMs in short-term exposure when compared to those without. We also found that ambient exposure to PM2.5 and PM10 could contribute to septic emboli

in IE patients. To the best of our knowledge, this investigation is the first study to explore the association of short-term exposure to PMs with septic emboli in IE.

Septic emboli could increase the risk of critical sequelae and even mortality in IE, if not properly managed.[23] In the previous report, it was shown that about 12% to 40% of patients with IE experienced embolic events.[13] The frequency of location where septic emboli were found could vary in different surveys. In the literature review, central nervous system (48–65%) was the most common place to be affected by septic emboli in IE, followed by extremities (30%), spleen (19–30%), lung (14–25%), kidney (6–14%), bone and joint structures (11%), liver (3–11%), coronary vessels (6%) and so on.[23–25] Besides, previous studies revealed that patients with left-sided IE and lesion on the mitral valve had a higher risk of septic emboli when compared to those with right-sided IE and lesion on the aortic valve, respectively.[26,27] In our study, neither left-sided (crude OR: 0.88, 95% CI: 0.38–2.03, P = .764) nor mitral valve-involved (crude OR: 0.87, 95% CI: 0.37–2.06, P = .752) IE has increased likelihood of septic emboli. Besides, it was reported that those who had IE due to Staphylococcus aureus, Streptococcus bovis or fungal infections or with vegetations sized over 10 mm could have a higher risk of experiencing embolic events.[28,29] In our study, IE Patients with MRSA infection were prone to have septic emboli when compared to those without, and there was no significant difference after adjustment with confounding variables in multivariate logistic regression. Notably, we found that the age of 65 years and more was significantly reversely associated with septic emboli in IE, which was somewhat different from the literature reviews.[30,31] This could be explained that the age of patients developing septic emboli in IE seemed to be younger (mean: 37.2 years; standard deviation: 12.4 years) in our study population when compared with that reported (mean: 38.1–46.3 years; standard deviation: 14.7–19.5 years) in the previous study.[30] And whether ambient exposure to air pollutants contributed to septic embolization in IE had not been explored yet in the previous studies.

PM2.5 and PM10, of which aerodynamic diameter less than 2.5 and 10 mm, respectively, were mainly composed of sulfate, nitrate, ammonium, organic and elemental carbons, trace metals, geological materials, and so on.[32,33] The significant impact of PM2.5 on health has been reported, affecting the occurrence and outcomes in a spectrum of diseases. Either long-term or short-term PM exposure was focused and investigated in the previous studies. In the surveys concerning short-term PM exposure, it was observed that ambient exposure to high PM2.5 concentrations for lag 0 through lag 1 day increased the risk of hospital admission and subsequent management because of OHCA, ischemic stroke, cardiovascular and respiratory diseases.[1,3–5,7] Besides, it was suggested that the level of PM2.5 at lag 2 day affected the outcomes of respiratory infection to the greatest extent.[1] In the present study, we also investigated the short-term effect of PM2.5 and PM10 on events of septic emboli in IE. Our results revealed that exposure to both high PM2.5 and PM10 levels for lag 0 through lag 2 day was associated with septic embolization in IE patients. However, the detailed mechanism of PM exposure facilitating septic embolization in IE remains to be explored. Researchers found that airborne microbes such as bacteria, fungi and viruses were identified in the composition of PM2.5 and PM 10 via DNA detection and sequencing analysis.[34] Besides, another study revealed that PM2.5 exposure contributed to pneumococcal adhesion to human epithelial cells,

thereby increasing the risk of pneumococcal pneumonia.[35] Nevertheless, the current evidence is insufficient to explain why IE patients exposed to high PM2.5 and PM10 levels have increased risk of developing septic emboli. One of the possible explanations is that PM-induced chronic inflammation could increase susceptibility to septic embolization in IE. The association of exposure to air pollutants with septic embolization in IE should be interpreted very carefully.

The impact of PM2.5 on health and the involved mechanism have been investigated and proposed. Prior studies indicated that PM2.5 triggered inflammatory response, oxidative stress and mitochondrial dysfunction in animal and cell line models.[36–38] Furthermore, it was demonstrated that acute PM exposure increased plasma expression of proinflammatory cytokines including interleukin (IL)-6 and tumor necrosis factor (TNF)-alpha, and activated polymorphonuclear leukocytes systemically.[39] Another study revealed that PM2.5-induced inflammatory response was suppressed by endotoxin neutralizer and knock-out of toll-like receptor (TLR)-4, while oxidative stress was not. Additionally, antioxidant treatment suppressed PM2.5-induced oxidative stress rather than the inflammatory response.[40] Although the above results suggested that environmental PM2.5 elicited systemic inflammation and oxidative stress by separate pathways, the link between PM2.5-induced inflammation with affected immunity and septic embolization remains to be disclosed; and further investigation remains warranted.

There are several major limitations in the present study. First, this is a retrospective study design in a single medical center and thus the case number is limited. Besides, the measured PM levels could have been inadequate indices of actual exposure in individuals due to the unavailability of indoor air quality, leading to overestimated or underestimated correlation between environmental PMs and septic embolization in IE.

5. Conclusions

In the present study, we demonstrated that IE patients with septic emboli and positive findings in blood culture were exposed to a significantly higher level of PMs in short-term exposure when compared to those without. Our results also suggested that the exposure to PM2.5 and PM10 contributed to septic emboli in IE.

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