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Review

Air particulate matter pollution and circulating surfactant protein: A systemic review and meta-analysis

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HIGHLIGHTS

- Comprehensive analysis on circulating surfactant proteins and air particulate matter in population.
- PM exposure was associated with a reduction of circulating SP-D.
- Circulating surfactant protein can be a biomarker for respiratory injury caused by particulate matter.

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ABSTRACT

Objective: Air particulate matter (PM) pollution is associated with the alterations in circulating pulmonary damage proteins. But there are not consistent results among the epidemiological studies. The aim of this study is to investigate the alteration of surfactant protein (SP) from PM exposure.
Methods: We conducted a comprehensive meta-analysis by searching the databases of PubMed, Medline, EMBASE, Web of Science and CNKI before October 2020 which reported PM pollutants and surfactant protein in the population. The sources of heterogeneity were assessed by subgroup (smoking, particulate matter with different aerodynamic diameter, exposure duration) analysis. We also used the publication bias tests for the comprehensive assessment.
Results: This meta-analysis consisted of 10 studies with 1985 subjects. The results showed that the combined standardized mean difference (SMD) value was 0.05, 95% confidence interval (CI) was −0.07 to 0.17 for serum SP-A and −0.81 (95% CI: -1.41 to −0.21) for circulating SP-D. Among smokers, the combined SMD value of SP-A were 0.29 (95% CI: 0.05 to 0.52). We did not find the correlation between publication year of SP-A and SP-D and study heterogeneity.
Conclusions: Circulating SP-D was significantly decreased by air particulate matter. Serum SP-A was significantly increased by PM exposure among smokers. Circulating surfactant protein may be considered as a biomarker for respiratory injury caused by air particulate matter.

Contents

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1. Introduction

Air pollution is one of the top 10 health threats from the World Health Organization's report in 2019. Exposure to particulate matter (PM) is associated with the global burden of disease and non-accidental mortality (Burnett et al., 2018). A growing number of studies suggest that PM can induce respiratory diseases, lung cancer and cardiovascular events (Berhane et al., 2016; Eckel et al., 2016; Zhao et al., 2020). A significant correlation between chronic obstructive pulmonary disease (COPD) mortality and PM exposure has been estimated (Lee et al., 2020). A recent 18-year cohort study further confirmed that exposure to ambient air pollutants was significantly associated with increasing emphysema (Wang et al., 2019). Mortality of respiratory disease consistent increase with increasing inhalable particulate matter concentration (Liu et al., 2019).

Emerging evidence suggest that biomarkers for pulmonary damage have been detected in peripheral circulation, especially in serum (Agassandian et al., 2014; Maher et al., 2017; Kahn et al., 2018). A good serum biomarker is expected to improve the specificity and sensitivity of health injury prediction and diagnosis (Liu et al., 2017; Chen et al., 2019). Both surfactant protein A (SP-A) and surfactant protein D (SP-D) are member of the collecting family, which mainly synthesized by the alveolar epithelium, and they play a pivotal role in alveolar innate immunity (Haagsman and Diemel, 2001; Hiroki et al., 2006). They are involved in manipulating cytokine and chemokine profiles in the inflammatory process (Kishore et al., 2006), and their levels in serum and plasma may potentially serve as biomarkers of lung disease or injury (Pastva et al., 2007). SP-D can regulate alveolar homeostasis (Zhang et al., 2006), macrophages, lymphocytes and reactive oxygen species (ROS) networks (Jaw and Sin, 2012). Some studies found elevated circulating SP-A and SP-D levels by the increased alveolar capillary permeability of patients (Bowler et al., 2004; Brasch et al., 2004). Under pathophysiological conditions, declining SP-A synthesis by alveolar capillary cells leads to lower lung SP-A and higher serum SP-A content (Yang et al., 2019). However, serum concentrations of SP-D may decrease after chronic damage to the airways, due to the decrease in the number of airway Club cells (Freberg et al., 2016) and the degradation of surfactant proteins by nitrosylation and oxidative damage during inflammation (Winkler et al., 2011; Atochina Vasserman et al., 2015).

Circulating SP-A and SP-D show variations in the serum of patients with different lung diseases and subjects exposed to lung toxicants (Hermans and Bernard, 1999). The reproducibility was better for SP-D levels in serum compared to bronchoalveolar lavage fluid (Winkler et al., 2011). Therefore, SP-A and SP-D may be promising biomarkers for pulmonary damage in disease prevention and health risk assessment. Nevertheless, the correlation between respiratory damage caused by atmospheric particles and specific biomarkers has not been clear. There is a lack of concordance and certainty (Suhaimi and Jalaludin, 2015; Siroux and Crestani, 2018). To fill the aforementioned gap and better evaluate the damaging effect of PM, we retrieve SP-A or SP-D studies associated with air pollution in population. Meta-analysis was used to analyze the correlation between particulate exposure and surfactant protein, providing a basis for health assessment.

2. Methods

2.1. Literature retrieval

A systematic literature retrieval was conducted in the database of PubMed, Medline, EMBASE, Web of Science and CNKI to identify appropriate studies before October 31, 2020. We used "AND" and "OR" to combined the key search terms in the format (("air pollution" OR "particulate matter" OR "PM2.5" OR "PM10") AND ("surfactant protein" OR "surfactant associated protein") AND ("blood" OR "serum" OR "plasma")) and mapped these terms to each database. What's more, hand-searched references that have been included in the articles were supplemented.

2.2. Study selection and review

2.2.1. Selection criteria

Eligible studies were selected through consideration of the title and abstract by two researchers independently. Disagreements were discussed by two researchers or resolved by the third researcher. The appropriate article was read in full to identify which studies were eventually included.

Concrete inclusion criteria in the meta-analysis include: (1) eligible studies which published between the database

establishment date and October 2020; (2) the design type include cross-sectional study, cohort study and randomized controlled trial associated with air pollution; (3) the subjects were human being, not cells or animals, and inclusion criteria for the study population were noted; (4) studies stratified by smoking and drinking need to have a clear definition of smoking and drinking; (5) the type of exposure of the air pollution component was marked and assessed. Notably, some studies were excluded: (1) the type of study design is inconsistent with the purpose of the study; (2) studies in languages other than English or Chinese; (3) the required data cannot be extracted into a unified form from the article; (4) for the repeated population studies, only the most complete published article has been included.

2.2.2. Quality assessment

Results of the quality assessment were presented in Table 1. We assessed cross-sectional study, cohort study and randomized controlled trial quality by AHRQ (Agency for Healthcare Research and Quality), Newcastle-Ottawa Scale and CASP Checklist (which was developed by the Critical Appraisal Skills Programme), respectively. And the above quality assessments were completed by two researchers independently, and the disagreement was discussed.

2.3. Data extraction

The information extracted from the article was as follows: title, first author, country, publication year, study design, sample size, the concentration (such as mean, standard deviation, interquartile range, *P*-value, median, maximum or minimum, etc.) of SP-A and SP-D, journal, the type of particulate matter, exposure duration.

2.4. Statistical analysis

As discussed by most of the researchers, the short-term exposure was defined by exposure period shorter than six months, while those exposed for more than six months were taken as long-term exposure. Additionally, current smokers were defined as those who still smoked at the time of the interview, and non-current smokers were subjects who did not smoke and had stopped smoking more than 12 months earlier.

We used Excel to record data, and the "meta" package in the statistical software R was used for meta-analysis. The concentration of SP-A and SP-D were entered as continuous variables. The data can eventually be directly or indirectly transformed into mean and standard deviation. In the initial phase of pooled analysis, we used a fixed effects model to combine each study. The heterogeneity was analyzed using the χ^2 test, with $P < 0.05$ to indicate significant statistical heterogeneity among each study. If significant heterogeneity was observed ($I^2 > 50\%$, $P < 0.05$), we used random effects model to analysis. The sources of heterogeneity were assessed by subgroup analysis (such as smoking, particulate matter with different aerodynamic diameter, exposure duration). Meta regression test was used to check whether the publication year was related to heterogeneity. Publication bias and sensitivity analysis were used to assess the effect of different studies on the combined effect size.

3. Results

3.1. Description of included studies

As shown in Fig. 1, a total of 2618 potential studies were identified by using different combination of key terms based on the published articles in five databases. Among them, 10 studies with 1985 subjects were considered to be eligible for meta-analysis. The basic information and quality assessment score of articles were shown in Table 1.

3.2. Meta-analysis

3.2.1. The alterations of circulating SP-A and SP-D by PM exposure

There were 10 articles included in the analysis, five studies evaluated changes of serum SP-A attributed to PM, eight of circulating SP-D. The meta-analysis results of SP-A and SP-D were shown in Fig. S1A and Fig. S1B. We found that PM exposure was significantly correlated with circulating SP-D reduction, but no correlation was found with SP-A.

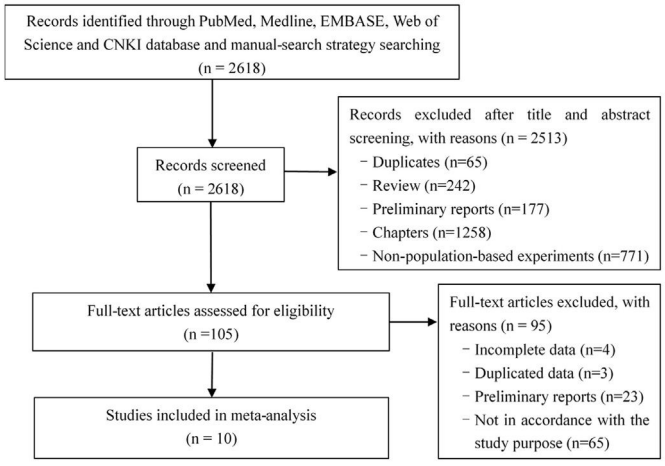

Fig. 1. Study selection diagram.

Table 1
Basic information about the studies included in the meta-analysis.

Reference	Design	Country	N	Biomarker	$PM_{2.5}$ (μg/m^3)		PM_{10} (μg/m^3)		Score
					Control group	Exposed group	Control group	Exposed group	
Berthoin K (Berthoin et al., 2004)	Cross-Sectional study	Belgium	112	SP-A	–	–	13.00	33.50	10
Heldal KK (Heldal et al., 2013)	Cross-Sectional study	Norway	82	SP-A, SP-D	–	–	–	310.00	10
Van Miert E (Van Miert et al., 2012)	Cross-Sectional study	Belgium	452	SP-D	–	–	–	–	10
Freberg BI (Freberg et al., 2016)	Cross-Sectional study	Norway	45	SP-A, SP-D	–	3100.00	–	6200.00	10
Wang Y (Wang et al., 2018)	Cross-Sectional study	China	768	SP-A, SP-D	62.60	168.15	–	–	10
Ellingsen DG (Ellingsen et al., 2019)	Cross-Sectional study	Norway	144	SP-D	–	–	–	8100.00	10
Yang M (Yang et al., 2019)	Cross-Sectional study	China	214	SP-A	1630.00	14900.00	–	–	10
Ellingsen DG (Ellingsen et al., 2015)	Cohort Study	Norway	140	SP-D	–	604.00	–	–	9
Albin M (Xu et al., 2013)	Randomized controlled trial	Sweden	18	SP-D	–	276.00	–	–	11
Ferguson MD (Ferguson et al., 2016)	Randomized controlled trial	America	10	SP-D	–	375.00	–	–	11

3.2.2. Circulating SP-A and SP-D changes with different aerodynamic diameter of particulate matter

Among five studies of serum SP-A attributed to PM, there were three of $PM_{2.5}$ and four of PM_{10}. Meta-analysis results were shown in Fig. 2 A. The heterogeneity test showed that there was no statistical heterogeneity among the studies ($I^2 = 0.0\%$, $P > 0.05$). Therefore, fixed effects model was used for the pooling analysis. The SMD value was 0.08 (95%CI: -0.05 to 0.21) in $PM_{2.5}$, and −0.05 (95%CI: -0.25, 0.15) in PM_{10}, respectively.

There were eight studies of circulating SP-D and PM, seven for

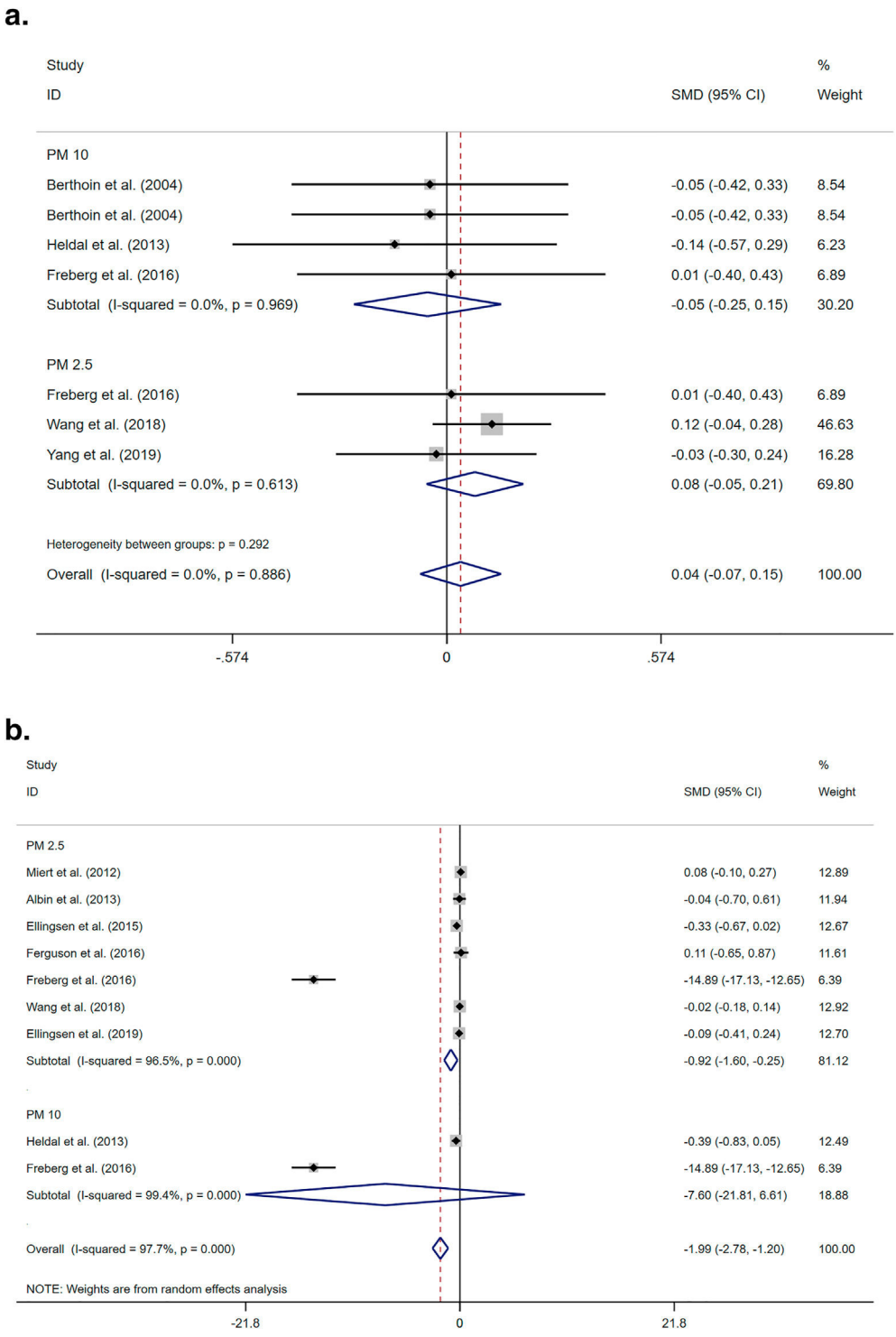

Fig. 2. Meta-analysis of circulating SP-A (A) and SP-D (B) with particulate matter of different aerodynamic diameters. **Notes:** The diamond shape is the combined standardized mean difference (SMD). Which is calculated as the difference in means between exposed group and control group, divided by the pooled standard deviation of the two means. The transverse diameter of the diamond represents the confidence interval for SMD; the horizontal line in the center of the graph is the confidence interval for each study; the squares represent the relative weights of each study; the dotted line is the effect line; the solid black line is the invalid line. If the confidence interval of the combined SMD was across the invalid line, the difference between the exposed group and the control group was not statistically significant.

$PM_{2.5}$ and two for PM_{10}. The meta-analysis results were shown in Fig. 2B. The heterogeneity test showed that there was significant statistical heterogeneity among the studies ($I^2 = 97.7\%$, $P < 0.05$). We used random effects model for the pooling analysis. The SMD value was −0.92 (95%CI: -1.60, −0.25) in $PM_{2.5}$, and −7.60 (95%CI: -21.81, 6.61) in PM_{10}. Therefore, there was a statistically significant reduction of circulating SP-D by $PM_{2.5}$ exposure.

3.2.3. Serum SP-A changes with particulate matter in smoking population

There were three studies of serum SP-A in smoking population. The two studies of circulating SP-D did not accurately assess the effects of smoking, so we only performed a subgroup analysis on serum SP-A. We used random effects model for the pooling analysis, and the smoking stratification analysis of SP-A was shown in Fig. 3. The SMD value was 0.21 (95% CI: 0.02 to 0.41) and 0.39 (95% CI: -0.15 to 0.93) among smokers and non-smokers with PM exposure, respectively. Above all, PM can induce the increase of serum SP-A among smokers.

3.2.4. Circulating SP-A and SP-D changes with different exposure duration of PM

Among five studies of serum SP-A and PM exposure duration, only one of them was less than 6 months. The meta-analysis results were shown in Fig. 4A, and there was no significantly statistical heterogeneity among the long-term exposure studies ($I^2 = 0.0\%$, $P > 0.05$). The SMD value was 0.06 (95% CI: -0.06 to 0.18).

There were eight studies which evaluated changes of circulating SP-D with PM exposure, and five studies for longer than 6 months, three for less than 6 months. The meta-analysis results were shown in Fig. 4B. The heterogeneity test showed that there was significantly statistical heterogeneity among the studies ($I^2 = 96.0\%$, $P < 0.05$). We used random effects model for the pooling analysis. The SMD was −1.37 (95%CI: -2.21, −0.54) in long-term exposed population, while the SMD was −0.21 (95%CI: -0.54 to 0.12) in short-term exposed population. The above results showed that circulating SP-D concentration was decreased by long-term exposure to air PM.

3.3. Sensitivity analysis and publication bias

3.3.1. Meta-regression

The results of meta-regression with REML method showed that there was no statistical correlation between publication year of circulating SP-A and SP-D and study heterogeneity (z = 0.73 and −0.29, $P = 0.47$ and 0.77, respectively).

3.3.2. Sensitivity analysis

The results of sensitivity analysis of SP-A and SP-D were shown in Fig. 5A and Fig. 5B. The combined SMD value of SP-A was 0.05, (95% CI: -0.07 to 0.17) after one study was removed once a time. The combined SMD value of SP-D was −0.81 (95% CI: -1.41 to −0.21) after one study was removed. We found one study significantly influenced the combined SMD value of SP-D. Therefore, we conducted a publication bias analysis.

3.3.3. Publication bias

Funnel plot is a qualitative measure of publication bias. The analysis results were shown in Fig. 6A and Fig. 6B. However, the funnel plot is asymmetric, suggesting the possibility of publication bias. We analyzed 10 studies that were included in the meta-analysis. The reason that leads to the asymmetry of funnel plots may be caused by the small sample size of several studies.

4. Discussion

A total of 10 studies were identified by systematic literature retrieval and quality assessment in our meta-analysis. We aim to offer a comprehensive analysis of the epidemiological evidence between PM and surfactant proteins. Primarily, we performed a heterogeneity test and a random effects model to combine statistics for studies with higher heterogeneity. Then, sources of heterogeneity were assessed by subgroup analysis, meta-regression, sensitivity analysis, and funnel plot. Eventually, we found a significant

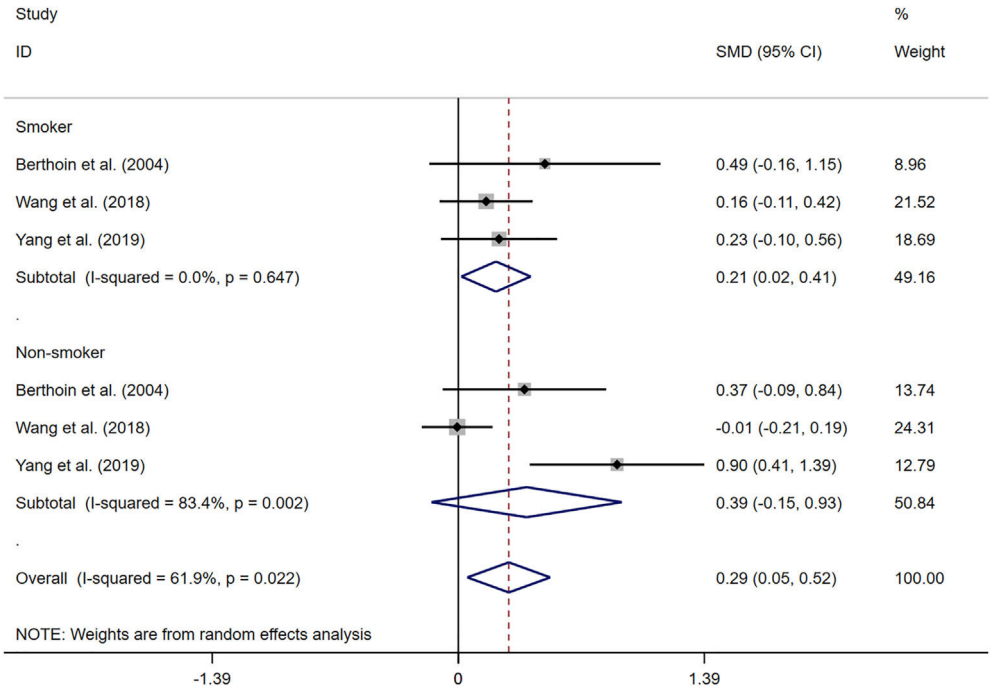

Fig. 3. Meta-analysis of serum SP-A changes among smokers with PM exposure.

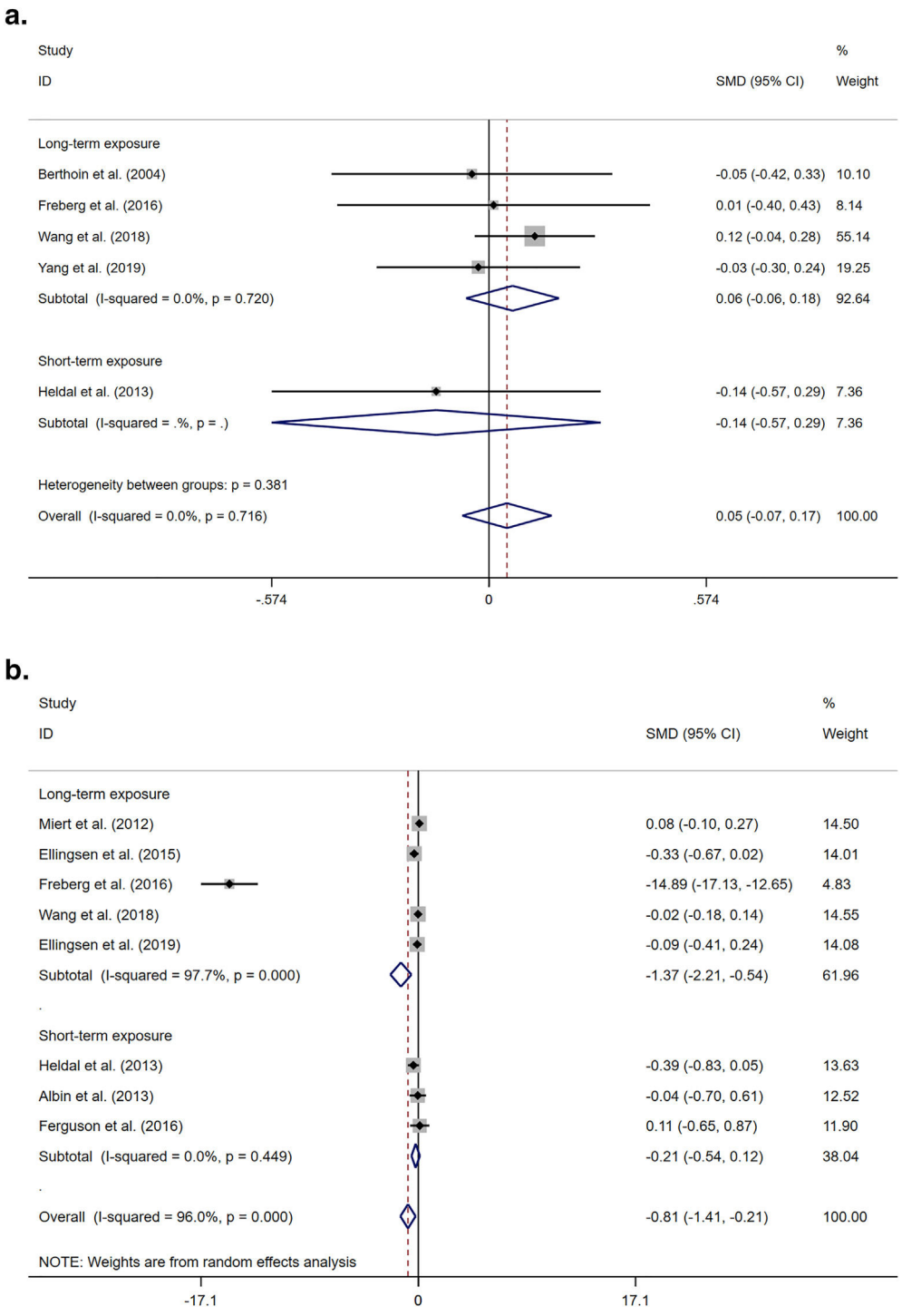

Fig. 4. Meta-analysis of circulating SP-A (A) and SP-D (B) changes with PM among different exposure duration population.

association between PM exposure and circulating SP-D changes in the primary meta-analysis, which remained in subgroup analysis. Furthermore, we found that there was no statistical correlation between publication year of SP-A and SP-D and study heterogeneity.

Epidemiological and toxicological studies have shown that PM can give rise to an extensive range of adverse effects. PM is associated with respiratory damage and even lung cancer incidence (Kelly and Fussell, 2015; Xing et al., 2019). Besides, experiments have shown that $PM_{2.5}$ components induced mitochondrial oxidative damage in lung cells and activated DNA damage responses in lymphocytes (Bhargava et al., 2018; Pardo et al., 2019). Dendritic cells can express toll-like receptors and c-type lectin receptors that have been shown to interact with SP-A and modulate inflammatory responses (Awasthi et al., 2011). SP-D is water-soluble and has collagen-like domains similar to SP-A (Kishore et al., 2006). It has been investigated that surfactant protein is essential for tissue-repair functions of macrophages, modulate the ROS (Casals et al., 2018; Peng et al., 2019).

Exposure to PM has been found to impair the expression of

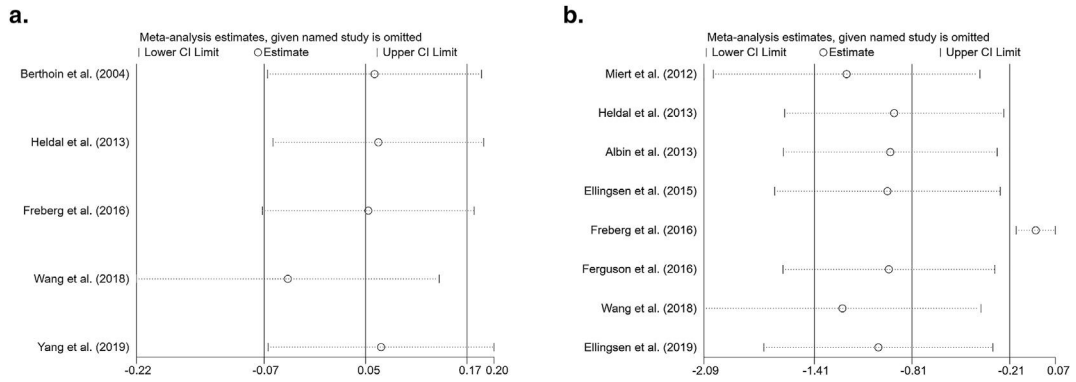

Fig. 5. Sensitivity analysis of circulating SP-A (A) and SP-D (B) with PM exposure.

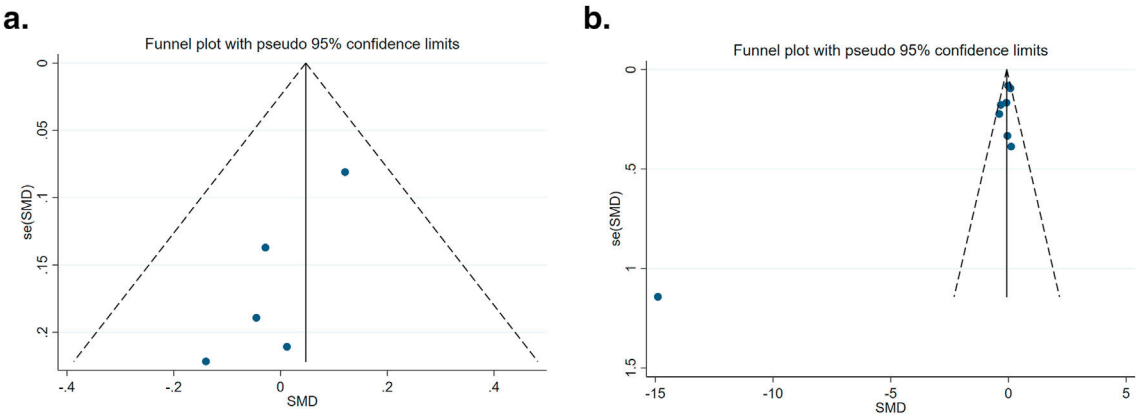

Fig. 6. Funnel plot of study-specific estimates of the SMD of SP-A (A) and SP-D (B) changes with PM exposure. **Notes:** If there is no publication bias, the point estimates for each study effect value are symmetrically distributed around the true value in an inverted funnel shape. If there is asymmetry or partial deletion, it indicates the possibility of publication bias.

surfactant protein (Silveyra and Floros, 2012). Our preliminary analysis did not find the correlation between PM and serum SP-A in population. Notably, subgroup analysis of smokers showed a significant increase of serum SP-A by PM exposure. A growing number of studies have shown that smoking is associated with respiratory damage and lung disease (Aghapour et al., 2018; Elicker et al., 2019). Wang (Wang et al., 2018) studied 768 people in China and found no significant change in serum SP-A and SP-D between the PM exposure population and the control group. However, Berthoin (Berthoin et al., 2004) conducted a study of 112 people in Belgium and found that all subjects have significantly higher SP-A levels among smokers. Elevated serum SP-A in smokers is likely to reflect increased permeability of the lung epithelium and damage to the distal airway cells caused by smoking. This hypothesis has been consistent with the findings of 214 Chinese PM exposed population (Yang et al., 2019). In animal studies, increased surfactant protein may play a protective role in the smoking-induced emphysema in mice by preventing alveolar cell death (Hirama et al., 2007).

Some epidemiological evidence suggest that the health impairments are related to the PM exposure duration (Lee et al., 2020). We conducted a stratified analysis of PM exposure durations, and we found decreased circulating SP-D in long-term exposed population, which was not found with SP-A. Freberg (Freberg et al., 2016) reported in a long-term PM exposure of 45 Norwegians, SP-D was significantly lower during the exposed days as compared with the non-exposed days. The decrease of surfactant protein may be the result of alveolar type II cell injury and altered synthesis of surfactant (Gregory et al., 1991). According to the reports by Berthoin (Berthoin et al., 2004) and Heldal (Heldal et al., 2013), no correlation was found between the alteration of SP-A and PM exposure duration. A study found that SP-D migrated and leaked into the blood more easily than SP-A by hydrophilicity and immunohistochemistry in rats (Nishikiori et al., 2014). Other studies observed that particles can inhibit the expression of SP-A in human alveolar type II cells (Correll et al., 2018; Dong et al., 2019).

We found a significant correlation between PM and circulating SP-D in the subgroup analysis stratified by different diameter of particulate matter. However, only $PM_{2.5}$ was associated with the reduction of circulating SP-D, while PM_{10} was not. Several latest studies showed that the all-cause mortality of $PM_{2.5}$ is higher than that of PM_{10} (Lu et al., 2015; Liu et al., 2019). Exposure to $PM_{2.5}$ has been associated with greater reductions in human birth weight than exposure to PM_{10} (Kumar, 2016). We inferred that this is related to the aerodynamic diameter. $PM_{2.5}$ can be inhaled deep into the lungs, but PM_{10} tends to be deposited in the upper parts of the human respiratory system (Ni and Zeng, 2013). It may suggest that the deep lung epithelium had not yet been affected by PM_{10}.

We performed a meta-analysis of circulating SP-A and SP-D, biomarkers of lung injury, caused by air particulate matter. Qualified studies were identified by systematic literature and quality assessment. Nevertheless, biomarkers for lung injury caused by PM are mainly focused on animal or cell experiments, and few studies meet our inclusion criteria. This also led to the fact that the pollutants of NO_X, PAHs were not carried out in this study, which may lead to differences in indicators from different compositions of PM in population.

5. Conclusion

Through the subgroup analysis of smoking, aerodynamic diameter and exposure duration of particulate matter, we found that circulating SP-D was significantly decreased by air particulate pollution. We also found serum SP-A was significantly increased by PM exposure among the smoking population. They may be considered as biomarkers for respiratory injury caused by air particulate matter pollution.

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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.chemosphere.2021.129564.

References

Agassandian, M., Shurin, G.V., Ma, Y., Shurin, M.R., 2014. C-reactive protein and lung diseases. Int. J. Biochem. Cell Biol. 53, 77–88.
Aghapour, M., Raee, P., Moghaddam, S.J., Hiemstra, P.S., Heijink, I.H., 2018. Airway epithelial barrier dysfunction in chronic obstructive pulmonary disease: role of cigarette smoke exposure. Am. J. Respir. Cell Mol. Biol. 58, 157–169.
Atochina Vasserman, E.N., Guo, C.J., Abramova, E., Golden, T.N., Sims, M., James, M.L., Beers, M.F., Gow, A.J., Krymskaya, V.P., 2015. Surfactant dysfunction and lung inflammation in the female mouse model of lymphangioleiomyomatosis. Am. J. Respir. Cell Mol. Biol. 53, 96–104.
Awasthi, S., Madhusoodhanan, R., Wolf, R., 2011. Surfactant protein-A and toll-like receptor-4 modulate immune functions of preterm baboon lung dendritic cell precursor cells. Cell. Immunol. 268, 87–96.
Berhane, K., Chang, C.C., McConnell, R., Gauderman, W.J., Avol, E., Rapapport, E., Urman, R., Lurmann, F., Gilliland, F., 2016. Association of changes in air quality with bronchitic symptoms in children in California. JAMA 315, 1491–1501, 1993-2012.
Berthoin, K., Broeckaert, F., Robin, M., Haufroid, V., De Burbure, C., Bernard, A., 2004. Serum pneumoproteins and biomarkers of exposure to urban air pollution: a cross-sectional comparison of policemen and foresters. Biomarkers : Biochem. Indicat. Expos., Response, Suscept. Chem. 9, 341–352.
Bhargava, A., Tamrakar, S., Aglawe, A., Lad, H., Srivastava, R.K., Mishra, D.K., Tiwari, R., Chaudhury, K., Goryacheva, I.Y., Mishra, P.K., 2018. Ultrafine Particulate Matter Impairs Mitochondrial Redox Homeostasis and Activates Phosphatidylinositol 3-kinase Mediated DNA Damage Responses in Lymphocytes.
Bowler, R., Duda, B., Chan, E., Enghild, J., Ware, L., Matthay, M., Duncan, M., 2004. Proteomic analysis of pulmonary edema fluid and plasma in patients with acute lung injury. Am. J. Physiol. Lung Cell Mol. Physiol. 286, L1095–L1104.
Brasch, F., Birzele, J., Ochs, M., Guttentag, S.H., Schoch, O.D., Boehler, A., Beers, M.F., Muller, K.M., Hawgood, S., Johnen, G., 2004. Surfactant proteins in pulmonary alveolar proteinosis in adults. Eur. Respir. J. 24, 426–435.
Burnett, R., Chen, H., Szyszkowicz, M., Fann, N., Hubbell, B., Pope, C.A., Apte, J.S., Brauer, M., Cohen, A., Weichenthal, S., Coggins, J., Di, Q., Brunekreef, B., Frostad, J., Lim, S.S., Kan, H., Walker, K.D., Thurston, G.D., Hayes, R.B., Lim, C.C., Turner, M.C., Jerrett, M., Krewski, D., Gapstur, S.M., Diver, W.R., Ostro, B., Goldberg, D., Crouse, D.L., Martin, R.V., Peters, P., Pinault, L., Tjepkema, M., van Donkelaar, A., Villeneuve, P.J., Miller, A.B., Yin, P., Zhou, M., Wang, L., Janssen, N.A.H., Marra, M., Atkinson, R.W., Tsang, H., Quoc Thach, T., Cannon, J.B., Allen, R.T., Hart, J.E., Laden, F., Cesaroni, G., Forastiere, F., Weinmayr, G., Jaensch, A., Nagel, G., Concin, H., Spadaro, J.V., 2018. Global estimates of mortality associated with long-term exposure to outdoor fine particulate matter. Proc. Natl. Acad. Sci. U. S. A. 115, 9592–9597.
Casals, C., Campanero-Rhodes, M.A., Garcia-Fojeda, B., Solis, D., 2018. The role of collectins and galectins in lung innate immune defense. Front. Immunol. 9, 1998.
Chen, F., Shu Xm, Fau, Wang, D.-x., Wang Dx, Fau, Xie, Y., Xie, Y Fau, Wang, G.-c., Wang, G.C., 2019. [Surfactant Proteins-A and D as Important Serum Markers for Interstitial Lung Disease in Patients with Polymyositis or Dermatomyositis.
Correll, K.A., Edeen, K.E., Zemans, R.L., Redente, E.F., Mikels-Vigdal, A., Mason, R.J., 2018. TGF beta inhibits expression of SP-A, SP-B, SP-C, but not SP-D in human alveolar type II cells. Biochem. Biophys. Res. Commun. 499, 843–848.
Dong, H., Zheng, L., Duan, X., Zhao, W., Chen, J., Liu, S., Sui, G., 2019. Cytotoxicity analysis of ambient fine particle in BEAS-2B cells on an air-liquid interface (ALI) microfluidics system. Sci. Total Environ. 677, 108–119.
Eckel, S.P., Cockburn, M., Shu, Y.H., Deng, H., Lurmann, F.W., Liu, L., Gilliland, F.D., 2016. Air pollution affects lung cancer survival. Thorax 71, 891–898.
Elicker, B.M., Kallianos, K.G., Jones, K.D., Henry, T.S., 2019. Smoking-related lung disease. Semin. Ultrasound CT MR 40, 229–238.
Ellingsen, D.G., Chashchin, M., Seljeflot, I., Berlinger, B., Chashchin, V., Stockfelt, L., Thomassen, Y., 2019. A study of atherothrombotic biomarkers in welders. Int. Arch. Occup. Environ. Health 92, 1023–1031.
Ellingsen, D.G., Ulvestad, B., Bakke, B., Seljeflot, I., Barregard, L., Thomassen, Y., 2015. Serum pneumoproteins in tunnel construction workers. Int. Arch. Occup. Environ. Health 88, 943–951.
Ferguson, M.D., Semmens, E.O., Dumke, C., Quindry, J.C., Ward, T.J., 2016. Measured pulmonary and systemic markers of inflammation and oxidative stress following wildland firefighter simulations. J. Occup. Environ. Med. 58, 407–413.
Freberg, B.I., Olsen, R., Thorud, S., Daae, H.L., Hersson, M., Molander, P., Barregard, L., Ellingsen, D.G., 2016. Pulmonary function and serum pneumoproteins in professional ski waxers. Inhal. Toxicol. 28, 7–13.
Gregory, T.J., Longmore, W.J., Moxley, M.A., Whitsett, J.A., Reed, C.R., Fowler 3rd, A.A., Hudson, L.D., Maunder, R.J., Crim, C., Hyers, T.M., 1991. Surfactant chemical composition and biophysical activity in acute respiratory distress syndrome. J. Clin. Invest. 88, 1976–1981.
Haagsman, H.P., Diemel, R.V., 2001. Surfactant-associated proteins: functions and structural variation. Comp. Biochem. Physiol. Mol. Integr. Physiol. 129, 91–108.
Heldal, K.K., Barregard, L., Larsson, P., Ellingsen, D.G., 2013. Pneumoproteins in sewage workers exposed to sewage dust. Int. Arch. Occup. Environ. Health 86, 65–70.
Hermans, C., Bernard, A., 1999. Lung epithelium–specific proteins. Am. J. Respir. Crit. Care Med. 159, 646–678.
Hirama, N., Shibata, Y., Otake, K., Machiya, J., Wada, T., Inoue, S., Abe, S., Takabatake, N., Sata, M., Kubota, I., 2007. Increased surfactant protein-D and foamy macrophages in smoking-induced mouse emphysema. Respirology 12, 191–201.
Hiroki, T., Hitomi, S., Hirofumi, C., Yoshio, K., 2006. Pulmonary surfactant proteins A and D: innate immune functions and biomarkers for lung diseases. Curr. Pharmaceut. Des. 12, 589–598.
Jaw, J.E., Sin, D., 2012. Unifying thoracic biomarkers: surfactant protein-D and beyond. Expet Rev. Respir. Med. 6, 147–154.
Kahn, N., Rossler, A.K., Hornemann, K., Muley, T., Grunig, E., Schmidt, W., Herth, F.J.F., Kreuter, M., 2018. C-proSP-B: a possible biomarker for pulmonary diseases? Respiration 96, 117–126.
Kelly, F.J., Fussell, J.C., 2015. Linking ambient particulate matter pollution effects with oxidative biology and immune responses. Ann. N. Y. Acad. Sci. 1340, 84–94.
Kishore, U., Greenhough, T.J., Waters, P., Shrive, A.K., Ghai, R., Kamran, M.F., Bernal, A.L., Reid, K.B.M., Madan, T., Chakraborty, T., 2006. Surfactant proteins SP-A and SP-D: structure, function and receptors. Mol. Immunol. 43, 1293–1315.
Kumar, N., 2016. The exposure uncertainty analysis: the association between birth weight and trimester specific exposure to particulate matter (PM2.5 vs. PM10). Int. J. Environ. Res. Publ. Health 13.
Lee, Y.M., Lee, J.H., Kim, H.C., Ha, E., 2020. Effects of PM10 on mortality in pure COPD and asthma-COPD overlap: difference in exposure duration, gender, and smoking status. Sci. Rep. 10, 2402.
Liu, C., Chen, R., Sera, F., Vicedo-Cabrera, A.M., Guo, Y., Tong, S., Coelho, M.S.Z.S., Saldiva, P.H.N., Lavigne, E., Matus, P., Valdes Ortega, N., Osorio Garcia, S., Pascal, M., Stafoggia, M., Scortichini, M., Hashizume, M., Honda, Y., Hurtado-Díaz, M., Cruz, J., Nunes, B., Teixeira, J.P., Kim, H., Tobias, A., Íñiguez, C., Forsberg, B., Åström, C., Ragettli, M.S., Guo, Y.-L., Chen, B.-Y., Bell, M.L., Wright, C.Y., Scovronick, N., Garland, R.M., Milojevic, A., Kyselý, J., Urban, A., Orru, H., Indermitte, E., Jaakkola, J.J.K., Ryti, N.R.I., Katsouyanni, K., Analitis, A., Zanobetti, A., Schwartz, J., Chen, J., Wu, T., Cohen, A., Gasparrini, A., Kan, H., 2019. Ambient particulate air pollution and daily mortality in 652 cities. N. Engl. J. Med. 381, 705–715.
Liu, J., Li, G., Li, L., Liu, Z., Zhou, Q., Wang, G., Chen, D., 2017. Surfactant protein-D (SP-D) gene polymorphisms and serum level as predictors of susceptibility and prognosis of acute kidney injury in the Chinese population. BMC Nephrol. 18, 67.
Lu, F., Xu, D., Cheng, Y., Dong, S., Guo, C., Jiang, X., Zheng, X., 2015. Systematic review and meta-analysis of the adverse health effects of ambient PM2.5 and PM10 pollution in the Chinese population. Environ. Res. 136, 196–204.
Maher, T.M., Oballa, E., Simpson, J.K., Porte, J., Habgood, A., Fahy, W.A., Flynn, A., Molyneaux, P.L., Braybrooke, R., Divyateja, H., Parfrey, H., Rassl, D., Russell, A.-M., Saini, G., Renzoni, E.A., Duggan, A.-M., Hubbard, R., Wells, A.U., Lukey, P.T., Marshall, R.P., Jenkins, R.G., 2017. An epithelial biomarker signature for idiopathic pulmonary fibrosis: an analysis from the multicentre PROFILE cohort study. Lancet Respir. Med. 5, 946–955.
Ni, H.G., Zeng, H., 2013. HBCD and TBBPA in particulate phase of indoor air in Shenzhen, China. Sci. Total Environ. 458–460, 15–19.
Nishikiori, H., Chiba, H., Ariki, S., Kuronuma, K., Otsuka, M., Shiratori, M., Ikeda, K., Watanabe, A., Kuroki, Y., Takahashi, H., 2014. Distinct compartmentalization of

SP-A and SP-D in the vasculature and lungs of patients with idiopathic pulmonary fibrosis. BMC Pulm. Med. 14, 196.
Pardo, M., Xu, F., Shemesh, M., Qiu, X., Barak, Y., Zhu, T., Rudich, Y., 2019. Nrf2 Protects against Diverse PM2.5 Components-Induced Mitochondrial Oxidative Damage in Lung Cells.
Pastva, A.M., Wright, J.R., Williams, K.L., 2007. Immunomodulatory roles of surfactant proteins A and D: implications in lung disease. Proc. Am. Thorac. Soc. 4, 252–257.
Peng, J., Zhang, L., Meng, Q., Zhang, F., Mao, X., Liu, J., Chen, Y., Zou, H., Shi, B., Wu, R., Huang, B., Huang, Y., Tan, J., Feng, C., Zhang, X., 2019. Adverse impact of ambient PM2.5 on expression and trafficking of surfactant protein A through reactive oxygen species damage to lamellar bodies. Toxicol. Lett. 315, 47–54.
Silveyra, P., Floros, J., 2012. Air pollution and epigenetics: effects on SP-A and innate host defence in the lung. Swiss Med. Wkly. 142, w13579.
Siroux, V., Crestani, B., 2018. Is chronic exposure to air pollutants a risk factor for the development of idiopathic pulmonary fibrosis? Eur. Respir. J. 51.
Suhaimi, N.F., Jalaludin, J., 2015. Biomarker as a Research tool in linking exposure to air particles and respiratory health. BioMed Res. Int. 1–10.
Van Miert, E., Sardella, A., Nickmilder, M., Bernard, A., 2012. Respiratory effects associated with wood fuel use: a cross-sectional biomarker study among adolescents. Pediatr. Pulmonol. 47, 358–366.
Wang, M., Aaron, C.P., Madrigano, J., Hoffman, E.A., Angelini, E., Yang, J., Laine, A., Vetterli, T.M., Kinney, P.L., Sampson, P.D., Sheppard, L.E., Szpiro, A.A., Adar, S.D., Kirwa, K., Smith, B., Lederer, D.J., Diez-Roux, A.V., Vedal, S., Kaufman, J.D., Barr, R.G., 2019. Association between long-term exposure to ambient air pollution and change in quantitatively assessed emphysema and lung function. J. Am. Med. Assoc. 322, 546–556.
Wang, Y., Duan, H., Meng, T., Shen, M., Ji, Q., Xing, J., Wang, Q., Wang, T., Niu, Y., Yu, T., Liu, Z., Jia, H., Zhan, Y., Chen, W., Zhang, Z., Su, W., Dai, Y., Zhang, X., Zheng, Y., 2018. Reduced serum club cell protein as a pulmonary damage marker for chronic fine particulate matter exposure in Chinese population. Environ. Int. 112, 207–217.
Winkler, C., Atochina-Vasserman, E.N., Holz, O., Beers, M.F., Erpenbeck, V.J., Krug, N., Roepcke, S., Lauer, G., Elmlinger, M., Hohlfeld, J.M., 2011. Comprehensive characterisation of pulmonary and serum surfactant protein D in COPD. Respir. Res. 12, 29.
Xing, D.F., Xu, C.D., Liao, X.Y., Xing, T.Y., Cheng, S.P., Hu, M.G., Wang, J.X., 2019. Spatial association between outdoor air pollution and lung cancer incidence in China. BMC Publ. Health 19, 1377.
Xu, Y., Barregard, L., Nielsen, J., Gudmundsson, A., Wierzbicka, A., Jönsson, A.A.B.A., Kåredal, M., Albin, M., 2013. Effects of diesel exposure on lung function and inflammation biomarkers from airway and peripheral blood of healthy volunteers in a chamber study. Part. Fibre Toxicol. 10, 60.
Yang, M., Li, Y., Meng, T., Zhang, L., Niu, Y., Dai, Y., Gao, W., Bloom, M.S., Dong, G., Zheng, Y., 2019. Ultrafine CB-induced small airway obstruction in CB-exposed workers and mice. Sci. Total Environ. 671, 866–873.
Zhang, L., Ikegami, M., Korfhagen, T.R., McCormack, F.X., Yoshida, M., Senior, R.M., Shipley, J.M., Shapiro, S.D., Whitsett, J.A., 2006. Neither SP-A nor NH2-terminal domains of SP-A can substitute for SP-D in regulation of alveolar homeostasis. Am. J. Physiol. Lung Cell Mol. Physiol. 291, L181–L190.
Zhao, B., Johnston, F.H., Salimi, F., Kurabayashi, M., Negishi, K., 2020. Short-term exposure to ambient fine particulate matter and out-of-hospital cardiac arrest: a nationwide case-crossover study in Japan. Lancet Planet. Health 4, e15–e23.