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REVIEW ARTICLE

Short-term exposure to particulate matter on heart rate variability in humans: a systematic review of crossover and controlled studies

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Abstract

As an indicator of cardiac autonomic function, heart rate variability (HRV) has been proven to decrease after short-term exposure to particulate matters (PM) based on controlled animal studies. In this study, we conducted a systematic review to investigate short-term effects of exposure with different particle sizes on HRV in humans. Both crossover and controlled studies of human which were published prior to February 2020 were searched on four electronic databases. The HRV parameters included standard deviation of normal-to-normal intervals (SDNN), root mean square of successive normal-to-normal intervals (RMSSD), percent of normal-to-normal intervals that differ by more than 50 milliseconds (PNN50), low frequency (LF), high frequency (HF), and LF/HF. This review included 14 studies with 300 participants. The short-term effects of PM exposure on HRV in humans are inconclusive. For time-domain parameters, one study showed higher SDNN values with 2-h exposure to PM, whereas another one showed lower SDNN values. One study found RMSSD increased after PM exposure. One study found PNN50 decreased after PM exposure. For frequency-domain parameters, two studies showed LF increased with 2-h exposure to PM, and two studies showed an increase of LF/HF after PM exposure. Four studies showed lower HF values after PM exposure, whereas two studies showed higher HF values. Five studies did not find statistically significant results for any HRV parameters. We could not conclude that short-term exposure to PM can influence autonomic nervous function. The inconsistent changes of HRV in response to PM exposure may have complex mechanisms, which remains to be elucidated.

Keywords Particulate matter · Heart rate variability · Crossover study · Controlled study · Systematic review · Human

Introduction

Cardiovascular disease (CVD) is a common disease that seriously impairs human health. The cases were estimated at 422 million worldwide and as the first leading cause of death, leading to one-third of all deaths in 2015 (Roth et al. 2017). In recent years, the level of air pollution has increased gradually (Bai et al. 2018). The public began to pay close attention to the relationship between air pollution and human health. Numerous studies have shown that both long-term and short-term exposure to particulate matters (PM) were associated with increased risk of CVD and its mortality (Cesaroni et al. 2014; Huang et al. 2016; Liu et al. 2018; Orellano et al. 2020). According to the estimate of World Health Organization (WHO), PM pollution caused approximately 3 million deaths around the world (World Health Organization 2016), and CVD was responsible for more than two-thirds of the deaths (Lelieveld et al. 2019).

Animal experiments are often used to investigate the mechanism of PM exposure on the cardiovascular system. Our previous meta-analysis of controlled animal experiments showed that PM exposure can lead to a decrease in heart rate variability (HRV) parameters, including standard deviation of normal-to-normal intervals (SDNN) and ratio of low frequency and high frequency (LF/HF), in rodents (Huang et al. 2020). As a reliable indicator of cardiac autonomic nervous regulation, reduced HRV has been suggested to be related to immune dysfunction and systematic inflammation, as well as an elevated risk of CVD (Chen et al. 2015; Kemp and

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Quintana 2013; Thayer et al. 2010). The animal experiments suggest that PM exposure may impact the course of CVD development via reducing HRV (Huang et al. 2020).

Meanwhile, epidemiological studies have been used to investigate associations of PM pollution and HRV in humans (Pieters et al. 2012; Buteau and Goldberg 2016). A review of cross-sectional and longitudinal studies concluded that there was evidence of a negative correlation between short-term exposure to PM and HRV, including LF, HF, SDNN, and root mean square of successive normal-to-normal intervals (RMSSD) (Pieters et al. 2012). However, a recent review of panel studies with repeated measurements of outcomes found limited evidence of the association, although negative associations of several HRV parameters and fine particles were found in older CVD patients (Buteau and Goldberg 2016).

Experimental studies with crossover design are also used to investigate effects of PM exposure on HRV indices in humans. Randomized crossover design can improve the quality of studies and provide more accurate evidence of the associations than observational studies. Several crossover studies have found short-term exposure to PM can lead to the decrease of HRV parameters, such as SDNN and HF (Brook et al. 2014; Graff et al. 2009; Vora et al. 2014). However, the results were inconsistent since some other studies found opposite or no statistically significant results (Byrd et al. 2016; Fakhri et al. 2009; Samet et al. 2009). At present, a systematic review of crossover studies is lacking. One previous review of crossover and prospective studies only included three crossover studies for ultrafine particles (UFPs) (Weichenthal 2012). Therefore, a systematic review designed to investigate effects of PM exposure with different particle sizes based on crossover studies for human is needed.

In this article, we conducted a systematic review of crossover and controlled studies to investigate short-term effects of exposure to PM with different particle sizes on HRV parameters in humans. HRV measurements included SDNN, RMSSD, LF, HF, LF/HF, and percent of normal-to-normal intervals that differ by more than 50 milliseconds (PNN50), which represents the changes of different nervous systems (Dong 2016).

Methods

Eligibility criteria

The aim of this systematic review was to examine short-term effects of exposure to PM on HRV in humans from crossover or controlled studies. The eligible study objects in this research were healthy participants or patients with a certain disease; PM exposures include UFPs, fine particles (particles that is 2.5 μm or less in diameter, $PM_{2.5}$), or coarse particles (particles that is 10 μm or less in diameter, PM_{10}), and at least one HRV parameter has been measured including SDNN, RMSSD, PNN50, LF, HF, and LF/HF. Studies targeted at multiple pollutants exposure or used other interventions simultaneously were excluded as these factors could be confounders in evaluating the effects of PM. We also excluded theses, dissertations, and research reports since they were not peer-reviewed.

Information sources and search strategy

Two English electronic databases (PubMed and EMBASE), and two Chinese electronic databases (CNKI and WanFang) were searched for related articles published before October 2020. The following search strategy was used in both English and Chinese articles: ("air pollution" OR "air pollutant*" OR "particulate matter*" OR PM OR PM_{10} OR $PM_{2.5}$ OR particle*) AND ("heart rate variability" OR HRV OR "heart period variability" OR "cycle length variability" OR "RR variability" OR "respiratory sinus arrhythmia" OR RSA OR "autonomic nervous system"). We did not use "study design" to search articles because this strategy was originally made to search all exposure studies, including controlled animal studies (Huang et al. 2020). We also identified studies by hand-checking reference lists of included studies and related reviews.

Study selection

Two independent researchers (FH and YZ) screened all articles searched. Firstly, titles and abstracts were reviewed to exclude irrelevant papers. We then read full texts of relevant papers and determined whether they should be included in the review according to the inclusion and exclusion criteria. Disagreements were resolved through discussion along with a third colleague (YL). Data was merged when it comes from the same population but different articles.

Data collection and items

Two independent researchers (FH and YZ) extracted the data from all studies included. Extracted information included study design (randomization, blinding method, wash out between exposure), participants information (health condition, age, gender, body mass index), exposure methods (particle size, concentration, way and duration of exposure, state during exposure), control methods, measurements (HRV indices, assessment time), and statistical methods.

Risk of bias

We assessed the risk of bias in the included studies from five aspects, which are allocation concealment (selection bias), blinding of participants (performance bias), blinding of

assessment (detection bias), incomplete outcome data (attrition bias), and wash out between exposure (a typical bias for crossover study). Risk of bias was rated as high, low, or unclear. The appraisal of the risk helps us better understand the quality of included studies.

Data analyses

Our initial goal was to conduct a meta-analysis. However, after reviewing the papers, we found the studies were different to a large extent in exposure (especially particle size and concentration) and participants (especially age and disease condition), which can lead to heterogeneity across studies. Furthermore, the measurement time, statistical method, and results expression of included studies varied dramatically, which makes it difficult to synthesize an overall effect. Therefore, we adopted a descriptive method to summarize the results.

Results

Characteristics of included studies

A total of 12 articles that represent 14 independent studies with 300 participants were included (Fig. 1) (Brook et al. 2014; Byrd et al. 2016; Devlin et al. 2014a, 2003b; Fakhri et al. 2009; Graff et al. 2009; Heusser et al. 2019; Huang et al. 2012; Samet et al. 2009; Tobaldini et al. 2018; Vora et al. 2014; Zareba et al. 2009).

Table 1 shows basic information about the included studies and participants. Thirteen studies adopted a randomized crossover design, and one adopted a randomized control design. Eleven studies were double-blind and the other three were single-blind. To eliminate the effects of previous exposure, washing out is needed in crossover study. All the crossover studies reported the use of washing out except one. The characteristics of participants varied considerably across studies. Participants in 11 studies were healthy, whereas the others were patients with specific diseases, including diabetes, metabolic syndrome, and asthma. Current nonsmokers were reported in thirteen studies. Male participants accounted for 60.3% in total and the mean age of the participants ranged from 24.9 to 66.9 years old.

Table 2 shows exposure and measurement information. Participants in 6 studies were exposed to UFPs, with mean concentration ranging from 10.0 to 98.0 μg/m^3; participants in three studies were exposed to coarse concentrated ambient particles (CAPs), with mean concentration ranging from 76.2 to 164.2 μg/m^3; participants in 4 studies were exposed to fine CAPs, with mean concentration ranging from 40.5 to 127.03

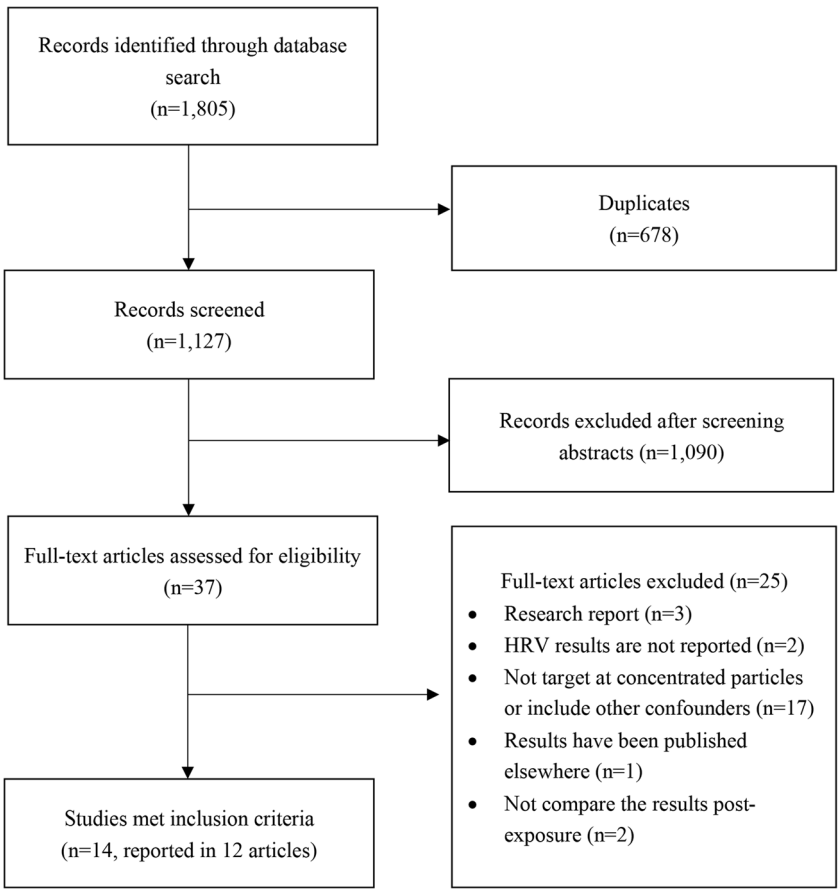

Fig. 1 Flow chart for selection of studies in the review

Table 1 Basic information of the studies and participants

Study	Design	Blinding	Wash out	Participants	Current smoker	N/No. of males	Age	BMI (kg/m^2)
Heusser et al. (2019)	Randomized crossover	Double-blind	Yes	Healthy, > 50 years	No	18/12	59.2 ± 7.0	27.3 ± 4.7
Tobaldini et al. (2018)	Randomized crossover	Double-blind	Yes	Healthy, young males	No	12/12	25.1 ± 2.2	18–28
Byrd et al. (2016)	Randomized crossover	Double-blind	Yes	Healthy, 18–50 years	No	29/20	30.4 ± 8.2	27.5 ± 6.0
Vora et al. (2014)	Randomized crossover	Double-blind	Yes	With type 2 diabetes, 30–60 years	No	17/9	45.9 ± 9.5	Male: 34.7 ± 5.2 Female: 31.1 ± 5.5
Devlin et al. (2014)	Randomized crossover	Double-blind	Yes	With MS, 27–70 years	No	19/13	47.8	/
Brook et al. (2014)	Randomized crossover	Double-blind	Yes	Healthy, 18–50 years	No	32/16	25.9 ± 6.6	26.3 ± 5.7
Huang et al. (2012)	Randomized crossover	Double-blind	Yes	Healthy, 20–36 years	No	23/15	24.6 ± 4.3	25.2 ± 3.1
Zareba et al. (2009)	Randomized crossover	Double-blind	Yes	Healthy, 18–40 years	No	12/6	30 ± 9	/
Zareba et al. (2009)	Randomized crossover	Double-blind	Yes	Healthy, 18–40 years	No	12/6	27 ± 6	/
Samet et al. (2009)	Randomized crossover	Double-blind	Yes	Healthy, 18–35 years	No	19/9	/	/
Graff et al. (2009)	Randomized crossover	Double-blind	Yes	Healthy, 18–34 years	No	14/8	24.9 ± 4.7	/
Fakhri et al. (2009)	Randomized crossover	Single-blind	Yes	With and without asthma, 19–48 years	No	50/24	27.08 ± 7.13	22.72 ± 3.24
Devlin et al. (2003)	Randomized control	Single-blind	/	Healthy, 18–40 years	No	CAPs: 22/17 FA: 11/7	CAPs: 28.8 ± 0.9 FA: 29.6 ± 1.1	/
Devlin et al. (2003)	Randomized crossover	Single-blind	Not given	Healthy, 60–80 years	Not given	10/7	66.9 ± 1.0	/

BMI, body mass index; *CAPs*, concentrated ambient particles; *FA*, filtered air; *MS*, metabolic syndrome

Table 2 Summary of the exposure and measurements

Study	Exposure					Control	HRV measurements
	Particles	Concentration ($\mu g/m^3$)	Way	Duration	State		
Heusser et al. (2019)	UFPs	68.5 ± 13.7	Whole body	3 h	Intermittent exercise	Filtered air	SD, RMSSD, LF, HF, LF/HF
Tobaldini et al. (2018)	Mixture	Fine: 33 Coarse: 48.6	Whole body	1 h	At rest	Filtered air	LF, HF, LF/HF
Byrd et al. (2016)	Coarse CAPs	164.2 ± 80.4	Whole body	2 h	At rest	Filtered air	SDNN, LF, HF, LF/HF
Vora et al. (2014)	UFPs	50	Mouthpiece	2 h	At rest	Filtered air	SDNN, RMSSD, PNN50, LF, HF, LF/HF
Devlin et al. (2014)	UFPs	98	Whole body	2 h	At rest	Clean air	SDNN, PNN50, LF, HF, LF/HF
Brook et al. (2014)	Coarse CAPs	76.2 ± 51.5	Whole body	2 h	At rest	Filtered air	SDNN, LF, HF, LF/HF
Huang et al. (2012)	Fine CAPs	89.5 ± 10.7	Whole body	2 h	Intermittent exercise	Clean air	SDNN, PNN50, LF, HF, LF/HF
Zareba et al. (2009)	UFPs	10	Whole body	2 h	At rest	Filtered air	SDNN, RMSSD, LF, HF, LF/HF
Zareba et al. (2009)	UFPs	10 and 25	Whole body	2 h	Intermittent exercise	Filtered air	SDNN, RMSSD, LF, HF, LF/HF
Samet et al. (2009)	UFPs	49.8 ± 20.0	Whole body	2 h	At rest	Filtered air	SDNN, RMSSD, PNN50, LF, HF, LF/HF
Graff et al. (2009)	Coarse CAPs	89.0 ± 49.5	Whole body	2 h	Intermittent exercise	Filtered air	SDNN, PNN50, LF, HF
Fakhri et al. (2009)	Fine CAPs	127.03 ± 62.13	Whole body	2 h	At rest	Filtered air	SDNN, RMSSD, PNN50, LF, HF, LF/HF
Devlin et al. (2003)	Fine CAPs	105.8 ± 12.6	Whole body	2 h	Intermittent exercise	Filtered air	SDNN, PNN50, LF, HF, LF/HF, TP
Devlin et al. (2003)	Fine CAPs	40.5 ± 8.6	Whole body	2 h	At rest	Filtered air	SDNN, PNN50, LF, HF, LF/HF, TP

CAPs, concentrated ambient particles; *HF*, high frequency; *HRV*, heart rate variability; *LF*, low frequency; *PNN50*, percent of NN intervals that differ by more than 50 milliseconds; *RMSSD*, root mean square of successive RR interval differences; *SD*, standard deviation of RR intervals; *SDNN*, standard deviation of the normal-to-normal RR intervals; *UFPs*, ultrafine particles

$\mu g/m^3$; participants in the remaining study were exposed to the mixture of fine and coarse particles. In terms of exposure way, one study adopted mouthpiece exposure, while all the others adopted whole body exposure. The duration of exposure was 2 h for most studies except two (one used 1-h exposure and the other one used 3-h exposure). Participants in 9 studies were at rest during exposure while participants in the other 5 studies were doing intermittent exercise. All studies used filtered or clean air as control.

Effects of short-term exposure to PM on HRV parameters

Table 3 exhibits the statistical methods and main findings of included studies. The results of time-domain measurements were not consistent across studies. Twelve studies assessed the short-term effects of PM exposure on SDNN. Among these studies, one showed higher SDNN values with exposure to UFPs when considered multiple time points. However, another study showed lower SDNN values 20 h after exposure to coarse CAPs. For RMSSD, 6 studies assessed the effects and one found RMSSD increased during, immediately, and 3 h after UFPs exposure. For PNN50, 8 studies assessed the effects and only one found PNN50 decreased immediately after fine CAPs exposure.

The short-term effects of PM exposure on LF and HF were assessed by all of the 14 studies. Two studies showed LF increased after UFPs exposure at 20-h and 18-h post-exposure time point. The results were not consistent for HF. Four studies showed lower HF values after PM exposure, including UFPs, coarse and fine CAPs. Two studies showed higher HF values after UFPs and fine CAPs exposure. Thirteen studies assessed LF/HF and two studies showed an increase at the time points of 0-h and 20-h post-exposure. Five studies did not find statistically significant results for any HRV parameters.

The statistical methods differed considerably across studies. Most studies collected and analyzed data at two or more time points while one study analyzed the data only at the time point of 1.5-h post-exposure. Paired t-tests were used to compare the observed outcomes at two time points in three studies, and analysis of variance and mixed model were used to compare the observed outcomes at multiple time points in 11 studies. Point values or the changes of HRV in form of difference

Table 3 Summary of statistical method and main findings

Study	SDNN	RMSSD	PNN50	LF	HF	LF/HF	Time point used to analyze	Significant time point	Statistical method	Results compared
Heusser et al. (2019)		o		o	o	o	1.5-h post-exposure	None	ANOVA	Point value
Tobaldini et al. (2018)				o	o	o	Pre, 0- and 2-h post-exposure	None	ANOVA	Point value
Byrd et al. (2016)	o			o	o	o	Pre and 0-h post-exposure	None	Paired t-tests	ΔHRV
Vora et al. (2014)	o	o	o	o	–	o	Pre, during, 0-, 3.5-, night, 21-, 45-h post-exposure	Multiple	Mixed model	ΔHRV
Devlin et al. (2014)	o		o	+	–	+	Pre, 1- and 20-h post-exposure or 24 h average	20-h post-exposure	Mixed model	Ratio (post/pre)
Brook et al. (2014)	o			o	–	+	Pre and 0-h post-exposure	0-h post-exposure	Mixed model	ΔHRV
Huang(2012)	o		o	o	o	o	Pre, 1- and 18-h post-exposure	None	Mixed model	Ratio (post/pre)
Zareba et al. (2009)	o	+		o	o	o	Pre, during, 0-, 3.5-, 15-, 21-h post-exposure	Multiple	ANOVA	ΔHRV
Zareba et al. (2009)	+	o		o	o	o	Pre, during, 0-, 3.5-, 15-, 21-h post-exposure	Multiple	ANOVA	ΔHRV
Samet et al. (2009)	o	o	o	+	+	o	Pre, 0- and 18-h post-exposure	18-h post-exposure	Mixed model	Ratio (post/pre)
Graff et al. (2009)	–		o	o	o		Pre, 0- and 20-h post-exposure	20-h post-exposure	Mixed model	ΔHRV
Fakhri et al. (2009)	o	o	o	o	+	o	Pre and 0-h post-exposure	0-h post-exposure	Mixed model	ΔHRV
Devlin et al. (2003)	o		o	o	o	o	Pre, 0- and 24-h post-exposure	None	Paired t-test	Ratio (post/pre)
Devlin et al. (2003)	o		–	o	–	o	Pre, 0- and 24-h post-exposure	0-h post-exposure	Paired t-test	Ratio (post/pre)

ANOVA, analysis of variance; *HF*, high frequency; *HRV*, heart rate variability; *LF*, low frequency; *PNN50*, percent of NN intervals that differ by more than 50 milliseconds; *RMSSD*, root mean square of successive RR interval differences; *SDNN*, standard deviation of the normal-to-normal RR intervals

+, increase; –, decrease; o, non-significant

a, statistically significant results are for exposure main effect; b, statistical significant results are for GSTM1 null subpopulation; c, statistically significant results are for exposure×xpos effect; d, statistically significant results are for 10 μg/m^3 exposure subgroup

and ratio of post-exposure to pre-exposure were exhibited in different studies.

Risk of bias

Figure 2 shows the risk of bias of included studies. The risk of selection bias qualified by allocation concealment and detection bias qualified by blinding of assessment were at a level of low for all studies. The risk of performance bias qualified by blinding of participants was high in three studies and low in the other studies. Attrition bias was serious for most studies since incomplete outcome data existed in eight studies. For the other bias, one crossover study did not report the use of washing out.

Discussion

HRV reflects autonomic nervous function and reduced HRV is considered an unfavorable prognostic biomarker for CVD (Bilchick et al. 2020; Tsuji et al. 1996). Altered cardiac autonomic nervous system control of heart rate could be one of the pathophysiological mechanisms by which PM affects the cardiovascular system. Our previous meta-analysis, based on 23 controlled animal studies, found short-term exposure to PM can lead to decrease of SNDD, LF, and LF/HF in rodents (Huang et al. 2020). Epidemiological evidence for human is inadequate. A meta-analysis of cross-sectional and longitudinal studies showed an inverse relationship between particulate air pollution and HRV parameters, including LF, HF, SDNN, and RMSSD (Pieters et al. 2012). However, a recent review of panel studies showed that the evidence is not enough to support the association (Buteau and Goldberg 2016). Crossover design is another common method to investigate the relationship of PM and HRV. Based on the review of 14 crossover/controlled studies, we did not find short-term exposure to PM had a specific effect on HRV.

For frequency-domain parameters, HF almost exclusively reflects parasympathetic function and variation of respiratory

Fig. 2 Risk of bias of the included studies

(Hayano et al. 1991; Task Force of the European Society of Cardiology 1996). We found the changes of HF after exposure were not consistent across studies. Four studies found HF decreased significantly during or after 2-h exposure to UFPs (Devlin et al., 2014; Vora et al. 2014), coarse (Brook et al. 2014), and fine CAPs (Devlin et al. 2003). These results support the hypothesis that short-term PM exposure can lead to impairment of parasympathetic autonomic function and reduced vagal tone. However, two other studies showed a statistically significant increase of HF after 2-h exposure to UFPs (Samet et al. 2009) and fine CAPs (Fakhri et al. 2009). The participants were aged 18–35 and 19–48, respectively. In contrast, the age of participants in previous 4 studies was 30–60, 27–70, 18–50, and 60–80. It is believed that HF is particularly sensitive to respiratory variation, and this respiratory influence is known to decrease with age (Hayano et al. 1991; Samet et al. 2009; Task Force of the European Society of Cardiology 1996). Therefore, the dichotomy in HF changes may result from the age difference of the studies.

Time-domain measurements RMSSD and PNN50 are also thought to reflect parasympathetic function (Aubert et al. 2003; Hayano et al. 1991; Rowan 3rd et al. 2007; Task Force of the European Society of Cardiology 1996). Six studies measured RMSSD and one study found RMSSD increased during and after UFPs exposure for healthy adults (Zareba et al. 2009). In contrast, eight studies measured PNN50 and one study found PNN50 decreased immediately following fine CAPs exposure for the elderly (Devlin et al. 2003). Meanwhile, more studies showed non-significant results of HF, RMSSD, and PNN50. Therefore, the association of short-term PM exposure and decreased parasympathetic function is inconclusive and needs to be further studied.

LF has been used as a marker of sympathetic function and LF/HF has been used as an index of sympathetic-vagal balance (Acharya et al. 2006; Rowan 3rd et al. 2007). Fourteen studies measured LF and 13 studies measured LF/HF. Two studies showed an increase in LF after exposure to UFPs (Devlin et al. 2014; Samet et al. 2009). Two studies showed an increase in LF/HF after exposure to coarse CAPs (Brook et al. 2014) and UFPs (Devlin et al. 2014). These results indicate sympathetic activation and/or vagal withdrawal. However, the results of SDNN, which may also have sympathetic influence (Hayano et al. 1991; Task Force of the European Society of Cardiology 1996), were not consistent. One study reported decreased SDNN values after exposure to 89.0 μg/m^3 coarse CAPs (Graff et al. 2009). Another study reported increased SDNN values with exposure to 10 μg/m^3 but not 25 μg/m^3 UFPs (Zareba et al. 2009). The authors argued that the concentration of PM might have an influence on the results. Most studies did not report significant results for LF, LF/HF, and SDNN, indicating that the association of PM exposure and sympathetic function is inconclusive and needs to be further studied.

A note of caution should be taken when interpreting these findings, especially the heterogeneity across studies. Firstly, the characteristics of participants and exposure were different. The participants from all of the fourteen studies include both the healthy and patients with certain diseases, all aged from 18 to 80 years old. PM exposure included ultrafine, fine, and coarse particles, and the concentration ranged from 10 to 127.03 μg/m^3. Secondly, the statistical methods varied considerably. Paired t-tests, mixed model, and analysis of variance were used to analyze the results. Different studies used different time points and the results were exhibited by different forms, including point value and changes of HRV calculated by subtracting or dividing the pre-exposure values. The heterogeneity makes it difficult to synthesize the results and draw a general conclusion. Furthermore, the exposure time was quite short (1–3 h). This may also have had an influence on the results.

Despite these limitations, the findings have practical implications. To our knowledge, this is the first systematic review of crossover and controlled studies to examine the effects of short-term exposure to PM on cardiac autonomic function, which was measured by HRV parameters in humans. Based on the current evidence, we cannot conclude that short-term exposure (1–3 h) to PM has an influence on autonomic nervous function. The inconsistent changes of HRV in response to PM exposure may have complex mechanisms, which remains to be elucidated.

Author contribution HF, YZ, and YL performed the literature search, HF and YL performed the data analysis and drafted the work, PW, YW, and LZ critically revised the work, and YL performed funding acquisition. All authors read and approved the final manuscript.

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Data availability Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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