Short-term effects of fine particulate matter on acute myocardial infraction mortality and years of life lost: a time series study in Hong Kong

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Abstract

Previous studies have applied years of life lost (YLL) as a complementary indicator to assess the short-term effect of the air pollution on the health burden from all-cause mortality, but sparsely focused on individual diseases such as acute myocardial infraction (AMI). In this study, we aimed to conduct a time-series analysis to evaluate short-term effects of fine particulate matter ($PM_{2.5}$) on mortality and YLL from AMI in Hong Kong from 2011 to 2015, and explore the potential effect modifiers including sex and age by subgroup analysis. We applied generalized additive Poisson and Gaussian regression model for daily death count and YLL, respectively. We found that per 10 $\mu g/m^3$ increment in concentration of $PM_{2.5}$ lasting for two days (lag_{01}) was associated with a 2.35% (95% CI 0.38% to 4.36%) increase in daily mortality count and a 1.69 (95%CI 0.01 to 3.37) years increase in YLL from AMI. The association between $PM_{2.5}$ and AMI mortality count was stronger among women and older people than men and young people, respectively. We concluded that acute exposure to $PM_{2.5}$ may increases the risk of mortality and YLL from AMI in Hong Kong and this effect can be modified by age and gender. These findings add to the evidence base for public health policy formulation and resource allocation.

Key Words

$PM_{2.5}$; AMI; mortality; years of life lost; time-series study; Hong Kong

1. Introduction

Cardiovascular disease (CVD) as the third leading cause of deaths in Hong Kong, accounted for 13.2% of all deaths in 2015; ischemic heart disease (IHD) as a major category was responsible for 66.6% of CVD deaths (Centre for Helath Protection, 2017). Acute myocardial infraction (AMI), as an important manifestation of IHD (Wichmann et al., 2014), is one of major public health concerns in Hong Kong and it is urgent to assess the burden of AMI and related risk factors.

Ambient air pollution is a large threat to public health in the world (WHO, 2016). Hong Kong is experiencing deteriorating air quality and the health impacts of air pollution might be even higher than those in the developing countries in South Asia (Wong et al., 2008). Fine particulate matter ($PM_{2.5}$), defined as atmospheric particulate matter with aerodynamic diameter $\leq 2.5\mu m$, is one of the principal air pollutants in Hong Kong. $PM_{2.5}$ is a mixture of various compounds including chemical and biological ingredients rather than a self-contained pollutant and is associated with a wide range of adverse health effects mainly including respiratory and cardiovascular diseases (Kim et al., 2015).

The short-term effects of $PM_{2.5}$ morbidity and mortality risk of AMI have been demonstrated in numerous

epidemiologic research studies in the world (Lanki et al., 2006; Nuvolone et al., 2011; von Klot et al., 2011; Wang et al., 2015; Wang et al., 2016; Wichmann et al., 2014). However, the short-term effect may differ because of the varying exposure level, components and the characteristic of population in different geographic locations (HEI, 2010). No studies have been conducted in Hong Kong to examine the association between acute exposure to $PM_{2.5}$ and AMI mortality. Moreover, mortality count alone depicts only a partial story of disease burden. Years of life lost (YLL), taking premature deaths and the life expectancy at death into consideration, would be an important complementary index to reflect the health burden due to air pollution, which is significant for public policy making and health service planning (Guo et al., 2013). Yet, studies applying YLL to quantify the disease burden have been sparse so far (Guo et al., 2013; He et al., 2016; Lu et al., 2015; Zhu et al., 2017) and to the best of our knowledge the short-term effect of $PM_{2.5}$ on YLL from AMI and the potential effect modification by demographic factors such as sex and age have not been investigated.

We performed a time-series study to evaluate the short-term effect of fine particulate matter on mortality and YLL from AMI, from 2011 to 2015 in Hong Kong, and explored the potential effect modification by sex and age.

2. Materials and methods

2.1 Data collection

2.1.1 Mortality data

Daily data on mortality due to AMI in Hong Kong from January 1, 2011 to December 31, 2015 were obtained from Hong Kong Census and Statistics Department (CSD). The anonymous records provided information such as sex, age, date of death, and underlying death cause which was coded according to the International Classification of Diseases, Tenth Revision (ICD-10). In this study, the daily mortality count from AMI (ICD-10: I21) was abstracted and stratified by sex and age group (≤65 and >65 years old). Since we only used aggregated data rather than individualised data in this study, ethics approval and consent from individual subjects were not required by our institute.

2.1.2 YLL data

Life tables for Hong Kong population from 2011 to 2014 were obtained from Hong Kong CSD (Census and Statistics Department, 2015), which provided the life expectancy at every exact age for males and females respectively. Life table for the year 2015 was unavailable, so we used life expectancies in 2014 as a substitute to compute the YLL for 2015. YLL values were calculated by matching sex and age to the life

tables and daily total YLL were calculated as the sum of YLL of all deaths due to AMI on the same day (Guo et al., 2013). The daily YLL data were also stratified by sex and age.

2.1.3 Air pollution and meteorology data

Hourly monitoring data for $PM_{2.5}$, particulate matter with aerodynamic diameters less than 10μm (PM_{10}), sulphur dioxide (SO_2), nitrogen dioxide (NO_2) and ozone(O_3) in 14 monitoring stations were collected by the Hong Kong Environmental Protection Department from 2011 to 2015. Excluding three roadside stations and one general station on a remote island, we used the data of the remaining 10 general stations to represent the general population exposure on a regular basis. We calculated the twenty-four hour mean concentrations of $PM_{2.5}$, PM_{10}, SO_2, NO_2 and O_3 for each station first and then averaged over ten stations to represent the daily exposure levels of the whole population. The daily mean temperature and relative humidity during 2011-2015 were obtained from the Hong Kong Observatory.

2.2 Statistical analysis

2.2.1 Spearman correlation

The correlation between air pollutants and meteorological conditions was evaluated by Spearman's rank correlation test.

2.2.2 Association between $PM_{2.5}$ and daily mortality count for AMI

We applied generalized additive Poisson regression model to estimate the association between daily mortality count for AMI and daily concentration of $PM_{2.5}$. We applied smoothing spline functions to control for secular trend and seasonality in daily mortality count, daily mean temperature, and relative humidity ($Humidity_0$). To adjust for the immediate and delayed effects of temperature, daily mean temperature of the same day ($Tmean_0$) the moving average of lag 1-3 days ($Tmean_{1-3}$) were included in the multiple regression model. The day of the week (*DOW*) and public holidays (*Holiday*) as dummy variables were also included in the model. Following the methods in previous studies (Bell et al., 2008; Peng et al., 2008; Qiu et al., 2012), we applied degrees of freedom (*df*) of 7/year for the time trend, 6 for $Tmean_0$ and $Tmean_{1-3}$, and 3 for relative humidity.The basic model was:

$$log(E(Y)) = \alpha + s(time, df = 7/year \times 5\ years) + s(Tmean_0, df = 6) + s(Tmean_{1-3}, df = 6)$$
$$+ s(Humidity_0, df = 3) + \beta_1 \times DOW + \beta_2 \times Holiday$$

where *E(Y)* represents the expected daily mortality count for AMI and *s(.)* the smoothing spline function for nonlinear variables. Residual plot and partial autocorrelation function (PACF) plot demonstrated the

successful control for secular trend and seasonality. The association of daily mortality count for AMI with $PM_{2.5}$ over two days, which was the moving average concentration over the same day and the previous day (lag_{0-1}) was included as the main analysis; association of AMI with $PM_{2.5}$ over the same day (lag_0) and three days before (lag_1 to lag_3) was also examined. We first fitted single pollutant models for $PM_{2.5}$ and the other three air pollutants (NO_2, SO_2 and O_3) and then included pollutants in multiple regression models. To find out whether there is effect modification by sex and age, we also examined the pollution and disease association in the subgroups and calculated the 95% confidence interval (CI) for difference: $(\beta_1 - \beta_2) \pm 1.96\sqrt{SE_1^2 + SE_2^2}$, where β_1 and β_2 are the estimates for two subgroups and SE_1 and SE_2 are their standard errors respectively (Schenker and Gentleman, 2001).

2.2.3 Association between $PM_{2.5}$ and daily YLL for AMI

We applied generalized additive Gaussian models to examine the association of $PM_{2.5}$ with YLL for AMI because daily YLL for AMI followed a normal distribution according to the previous studies (Guo et al., 2013; Zhu et al., 2017). In the current study, the distribution of YLL from AMI and the plot of model residuals showed that the normality was not violated (Figure S1).

All statistical analysis was performed with the *mgcv* package in R software, version 3.4.0. The results were presented in percent excess risk of daily mortality count (ER %) or the increment in YLL for AMI per 10μg/m^3 increase of $PM_{2.5}$.

3. Results

3.1 Descriptive statistics

During the 1,826 days from 1 January 2011 to 31 December 2015, a total of 9,252 deaths due to AMI were recorded. The means of daily deaths and YLL due to AMI were 5.1 cases and 68.3 person years, respectively. Both daily death counts and YLL were higher for men and older people (age>65 years old) than women and younger people (age≤65 years old), respectively (**Table 1**).

The daily mean concentration of $PM_{2.5}$ was 29.1μg/m^3, with a SD of 17.3μg/m^3. For the other air pollutants, the daily mean concentrations of PM_{10}, NO_2, SO_2 and O_3 were 43.7μg/m^3, 54.5μg/m^3, 11.6μg/m^3 and 40μg/m^3 respectively (**Table 1**). $PM_{2.5}$ was strongly correlated with PM_{10} (Spearman correlation coefficient r=0.98), NO_2 (r=0.74), and moderately correlated with O_3 (r=0.58) and SO_2 (r=0.41). Mean temperature and relative humidity were negatively correlated with $PM_{2.5}$ (**Table 2**).

Figure S2 shows the time trend and daily variation of air pollution as well as the mortality count and

YLL from AMI.

Table 1| Levels of daily $PM_{2.5}$, mean temperature, relative humidity, YLL and daily death counts for AMI in Hong Kong, China, 2011-15 (Number of days=1826)

	Minimum	25% quartile	Median	75% quartile	Maximum	Mean	Standard deviation
Pollution concentration ($\mu g/m^3$)							
$PM_{2.5}$	4.9	14.6	25.9	39.5	115.6	29.1	17.3
PM_{10}	7.6	23.9	38.8	57.9	157.4	43.7	23.8
NO_2	12.9	41	51.8	64.3	162.3	54.5	18.1
SO_2	3.3	7.5	10.4	14.3	46.9	11.6	5.8
O_3	4.7	20.6	34.1	55.3	134.4	40.0	23.6
Meteorology measures							
Mean temperature(°C)	8.4	19	24.8	28.2	32.4	23.5	5.3
Relative humidity (%)	29	74	79	85	99	78.3	10.3
YLL (years)							
Total	0	39.5	63.2	91.3	255.3	68.3	39.5
Women	0	7.9	18.4	33.9	109.7	23.2	20.1
Men	0	19.6	39.3	64.6	202.5	45.1	32.8
Age ≤65 years	0	0	24.8	48.0	175.0	30.2	31.5
Age >65 years	0	21.8	35.3	53.2	136.2	38.4	22.4
Daily death counts (No of deaths)							
Total	0	3	5	7	16	5.1	2.5
Women	0	1	2	3	9	2	1.5
Men	0	2	3	4	12	3	1.9
Age ≤65 years	0	0	1	2	6	1	1.1
Age >65 years	0	2	4	5	13	4	2.2

Abbreviations: YLL, year of life lost; $PM_{2.5}$, particles with an aerodynamic diameter less than 2.5 μm; PM_{10}, particles with an aerodynamic diameter less than 10 μm; NO_2, nitrogen dioxide; SO_2, sulphur dioxide; O_3, ozone.

Table 2| Spearman correlation between air pollutants and weather conditions in Hong Kong, China, during 2011–15

	PM_{10}	NO_2	SO_2	O_3	Mean temperature	Relative humidity
$PM_{2.5}$	0.98*	0.74*	0.41*	0.58*	-0.53*	-0.48*
PM_{10}	—	0.72*	0.40*	0.62*	-0.52*	-0.53*
NO_2	—	—	0.53*	0.29*	-0.43*	-0.32*
SO_2	—	—	—	-0.05	0.04	-0.48*
O_3	—	—	—	—	-0.16*	-0.47*
Mean temperature	—	—	—	—	—	0.11*

*P<0.01

Abbreviations: $PM_{2.5}$, particles with an aerodynamic diameter less than 2.5 μm; PM_{10}, particles with an aerodynamic diameter less than 10 μm; NO_2, nitrogen dioxide; SO_2, sulphur dioxide; O_3, ozone.

3.2 Modelling results

Table 3 presents the excess risk estimates in AMI mortality and YLL per 10μg/m^3 increase in $PM_{2.5}$ on different lag days in single pollutant models. $PM_{2.5}$ was associated with daily mortality on lag_0 and lag_1 days; the largest risk estimates were found with lag_{0-1}. The association between $PM_{2.5}$ and YLL was statistically significant at lag_{0-1}.

Table 4 summarizes the relationship between $PM_{2.5}$ at lag_{0-1} and AMI in single and co-pollutant models. An increment of $PM_{2.5}$ by 10μg/m^3 at lag_{0-1} was associated with 2.35% (95% CI: 0.38% to 4.36%) increase in daily mortality and 1.69 (95%CI: 0.01 to 3.37) years increase in daily YLL from AMI. SO_2 was also associated with increased risk of daily death and YLL from AMI, while no associations were found with NO_2 or O_3. In the co-pollutant models, the risk estimates for $PM_{2.5}$ changed slightly.

The exposure–response relationship was approximately linear, as seen in **Figure S3**.

Table 5 shows the excess risk estimates in AMI mortality and YLL per 10μg/m^3 increase in $PM_{2.5}$ at lag_{0-1} in single pollutant models for different sex and age groups respectively. The AMI mortality risk estimates were higher for women and elders than for men and young people, respectively. The association of $PM_{2.5}$ with YLL from AMI did not vary by sex or age group.

Table 3| Association between 10 µg/m^3 increase in $PM_{2.5}$ and YLL and increase in deaths for AMI by lags using single pollutant models during 2011-15*

Lag days	Increase in YLL(years)	ER of daily mortality count (%)
Lag0	1.47 (-0.05, 3.00)	**1.82 (0.04, 3.62)**
Lag1	1.20 (-0.26, 2.66)	**1.87 (0.16, 3.60)**
Lag2	0.59 (-0.83, 2.01)	1.13 (-0.53, 2.81)
Lag3	0.30 (-1.09, 1.69)	1.40 (-0.23, 3.05)
Lag01†	**1.69 (0.01, 3.37)**	**2.35 (0.38, 4.36)**

* Generalized additive Poisson model for mortality count and Gaussian model for YLL was applied and controlled for long-term trend, seasonality, weather factors, calendar effect. Statistically significant effect estimates are in bold.
†Overall cumulative effects of $PM_{2.5}$ lasting for 0–1 days were estimated
Statistically significant effect estimates are in bold.
ER, excess risk; $PM_{2.5}$, particles with an aerodynamic diameter less than 2.5 µm.

Table 4| Association between 10µg/m^3 increase in $PM_{2.5}$ (lag 0-1 day) and YLL and increase in deaths for AMI using single, two, and three pollutant models during 2011-15*

	Increase in YLL(years)	ER of daily mortality count (%)
Single pollutant model		
$PM_{2.5}$	**1.69 (0.01, 3.37)**	**2.35 (0.38, 4.36)**
NO_2	0.62 (-0.92, 2.17)	1.50 (-0.36, 3.39)
SO_2	**4.97 (0.28, 9.66)**	**6.64 (0.90, 12.7)**
O_3	-0.15 (-1.28, 0.99)	-0.19 (-1.56, 1.2)
Co-pollutant model		
+NO_2	1.66 (-0.19, 3.51)	1.48 (-0.63, 3.63)
+SO_2	0.87 (-0.91, 2.65)	1.01 (-1.06, 3.12)
+O_3	**1.77 (0.14, 3.41)**	**2.14 (0.25, 4.06)**
+NO_2+SO_2	1.29 (-0.60, 3.18)	1.09 (-1.08, 3.30)
+NO_2+O_3	**2.07 (0.07, 4.07)**	1.86 (-0.40, 4.17)
+SO_2+O_3	1.17 (-0.85, 3.19)	1.30 (-1.02, 3.68)

* Generalized additive Poisson model for mortality count and Gaussian model for YLL was applied and controlled for long-term trend, seasonality, weather factors, calendar effect. Statistically significant effect estimates are in bold.
ER, excess risk; $PM_{2.5}$, particles with an aerodynamic diameter less than 2.5 µm.

Table 5| Association between 10μg/m^3 increase in $PM_{2.5}$ (lag 0-1 day) and YLL and increase in deaths for AMI using the single pollutant model during 2011-15, according to sex and age*

	Increase in YLL(years)	ER of daily mortality count (%)
Gender		
Women	0.68 (-0.19, 1.55)	**4.05 (1.00, 7.18)**
Men	1.01 (-0.39, 2.41)	1.22 (-1.32, 3.82)
Age group		
Age ≤65 years	0.63 (-0.74, 2.01)	1.76 (-2.51, 6.21)
Age >65 years	0.93 (-0.01, 1.87)	**2.39 (0.23, 4.61)**

* Generalized additive Poisson model for mortality count and Gaussian model for YLL was applied and controlled for long-term trend, seasonality, weather factors, calendar effect. Statistically significant effect estimates are in bold.
Differences of the effect estimates between different sex and age group were not statistically significant.
ER, excess risk; $PM_{2.5}$, particles with an aerodynamic diameter less than 2.5 μm.

4. Discussion

This was the first study to examine the association of short-term $PM_{2.5}$ exposure with mortality and YLL from AMI. With the time-series data of 2011-2015 in Hong Kong, we found $PM_{2.5}$ was associated with an increase in AMI mortality and YLL due to AMI. The magnitude of $PM_{2.5}$ effect on AMI mortality appeared to be larger among women and older people with age > 65 years old.

The short-term association of $PM_{2.5}$ with AMI mortality was consistent with previous epidemiological studies (Mate et al., 2010; Sharovsky et al., 2004; Ueda et al., 2009; Zanobetti and Schwartz, 2009), although the mechanisms of the $PM_{2.5}$ effect remain not entirely clear. One of the major mechanisms may be oxidative stress and inflammation (Brook et al., 2010). $PM_{2.5}$ induces not only pulmonary oxidative stress and inflammation but also a systemic inflammatory response. After inhalation of $PM_{2.5}$, a local inflammatory response is developed and several proinflammatory mediators such as IL-6 and TNF-α are increased as well, which induces the increment in the concentrations of blood fibrinogen and C-reactive protein (CRP), which are important risk factors for AMI. Numerous studies have demonstrated that exposure to particulate matters is associated with increase of fibrinogen and CRP, resulting in an increased risk of AMI (Ghio et al., 2000; Pope et al., 2004; Ruckerl et al., 2007; Tornqvist et al., 2007). With the inflammation after exposure to $PM_{2.5}$, the haemostatic system can be activated abnormally

(Seaton et al., 1995) and the blood viscosity can be increased (Peters et al., 1997), which promotes acute thrombosis formation and atherosclerotic plaque.

$PM_{2.5}$ can also disturb autonomic nervous system (ANS), which is another potential mechanism of its association with AMI (Brook et al., 2004). Through decreased parasympathetic input to the heart, $PM_{2.5}$ is negatively associated with heart rate variability (HRV) (Devlin et al., 2003; Gong et al., 2004), which is a significant and independent predictor of mortality after an AMI (Electrophysiology, 1996). Another potential pathway is the direct translocation of $PM_{2.5}$ into circulatory system and cause an acute cardiovascular response. Reactive oxygen species (ROS) production and regulation of calcium levels are two major pathways of the direct cardiovascular effect (Fiordelisi et al., 2017). Endothelial cells are damaged especially by the specific metal components of $PM_{2.5}$ (Niu et al., 2013). Recently, increasing evidence (Bai et al., 2001; Okayama et al., 2006; Zuo et al., 2011) showed that ROS such as superoxide and hydrogen peroxide play a role in various situations including pulmonary and systemic inflammatory responses, vascular cytotoxicity and cardio myocyte dysfunction.

In the current study we estimated the YLL from AMI related to ambient $PM_{2.5}$ pollution, which was probably first such report. YLL, accounting for premature deaths and life expectancy, could provide more information on the scale of the loss of life and would be a more informative indicator to assess the health burden compared with mortality (Rabl, 2003). It would be an important complementary index for public policy making and health service planning (Guo et al., 2013). But it was argued that morality should be a typical indicator to demonstrate the health outcome while YLL could be a supplementary indicator to reflect the disease burden because YLL was less sensitive than mortality (Zhu et al., 2017). Furthermore, the normal distribution assumption for YLL can be violated, especially for the YLL from some specific disease categories and the YLL in the subgroup analyses, which may distort the true association between air pollution and YLL.

We could not directly compare the $PM_{2.5}$ associated YLL estimates for AMI in the current study with those from the previous studies in which all-cause mortality was the major health outcome (Guo et al., 2013; He et al., 2016; Zhu et al., 2017). Meanwhile, the magnitude of the association between $PM_{2.5}$ and YLL may also be related to the population size, which makes the results from different settings uncomparable. He T et.al (He et al., 2016) reported that a $10\mu g/m^3$ increase of $PM_{2.5}$ was associated with 2.97 (95%CI -2.01 to 7.95) years of YLL for all-cause mortality in Ningbo during 2009 to 2013. Yang J et.al (Yang et al., 2016) and Li G et.al (Li et al., 2016) explored the short-term effect of air pollution on YLL from CVD and IHD respectively, but $PM_{2.5}$ was not included in their analyses.

For the metric of AMI mortality, females and older people were found to be more susceptible to $PM_{2.5}$, which was consistent with previous observations on AMI morbidity and mortality (D'Ippoliti et al., 2003; Nuvolone et al., 2011). In 2010, the American Heart Association (AHA) statement concluded that women

may be at higher risk for cardiovascular mortality related to the particulate matter exposure (Brook et al., 2010). Regional deposition of inhaled particles could be enhanced in women (Kim and Hu, 1998). Women have fewer red blood cells (RBCs) compared with men, thus they would be more sensitive to the toxicological effects of airborne pollution (Sorensen et al., 2003). On the other hand, the elderly is also a high-risk group compared with the youth, which has been supported by AHA statement (Brook et al., 2004). The immune system might be weaker among older people and other chronic diseases might occur, which are the potential reasons for greater susceptibility among the elderly.

With co-pollutant adjustment in multi-pollutant models, the association of $PM_{2.5}$ with mortality and YLL from AMI decreased slightly, which may be due to the high correlation and the co-linearity between air pollutants. We observed approximately linear concentration-response relationship of ambient $PM_{2.5}$ exposure with both AMI mortality and YLL, which was consistent with a previous study by Samoli E (Samoli et al., 2005), in which the association between ambient particles and all-cause mortality in Europe was linear without a threshold.

The current study was based in one single city of Hong Kong and thus the issue of generalizability should be considered along with emerging evidence elsewhere. Outdoor monitoring data were used to approximate the total population exposure to air pollution, which would cause measurement error of the exposure level of $PM_{2.5}$, especially for the elderly and other subgroup populations who stay indoors longer. Therefore, the exposure to $PM_{2.5}$ might have been underestimated (Zeger et al., 2000) although Schwartz J et al.(Schwartz et al., 2007) found that the ambient pollutant concentration of $PM_{2.5}$ was reasonable surrogates for personal exposures.

Despite these limitations, there were two strengths in the present study. First, as the first study applying YLL as a complementary indicator to explore the short-term effect of $PM_{2.5}$ on death from AMI, the disease burden due to AMI could be assessed more precisely because the life expectancy at the age of death was incorporated in the calculation of YLL. Second, unlike the previous studies in which the life table applied to calculate YLL was not in accordance with the study period and the life expectancy was only provided for age groups of 5 years interval (Guo et al., 2013; He et al., 2016; Yang et al., 2016), the calculation of YLL in the current study was based on the corresponding life table of each year and life expectancy of each exact age, which improved precision of the YLL estimates.

In conclusion, acute exposure to $PM_{2.5}$ increased the mortality risk and YLL from AMI in Hong Kong. Moreover, age and gender modified the effect of $PM_{2.5}$ on AMI mortality. With the estimates of YLL, this study adds to the evidence base for public health policy formulation and resource allocation.

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