Biomarkers, 2009; 14(S1): 74–78

informa
healthcare

REVIEW ARTICLE

Residential traffic exposure and coronary heart disease: results from the Heinz Nixdorf Recall Study

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Abstract
Traffic is one of the major sources of environmental pollution in metropolitan areas, emitting pollutants such as particulate matter and noise. Epidemiological evidence links both particulate matter (PM) and noise to cardiovascular disease and increased cardiovascular mortality. Short-term exposure to traffic may trigger acute cardiovascular events. Long-term residential traffic exposure is associated with the degree of subclinical atherosclerosis, prevalence of coronary heart disease and incidence of myocardial infarction. This review will present recent epidemiological findings regarding long-term exposure to traffic and its association with coronary heart disease, using results from the Heinz Nixdorf Recall Study, an ongoing prospective cohort study of 4814 unselected participants living in three large adjacent cities of the highly industrialized Ruhr Area in western Germany. Special focus is placed on the association of long-term traffic exposure with subclinical atherosclerosis, the major underlying pathology for cardiovascular disease.

Keywords: *Epidemiology; traffic; particulate matter; coronary heart disease; atherosclerosis*

Introduction

Traffic is one of the major sources of environmental pollution in metropolitan areas, emitting traffic-generated particulate matter (PM), gaseous pollutants and noise. It contributes to a large extent to the intra-urban differences of PM and noise exposure in the general population. Epidemiological evidence links both PM and noise to an increased cardiovascular disease risk (Brook et al. 2004, Babisch, 2008).

It has been suggested that particles resulting from traffic exert higher cardiovascular toxicity than particles from other sources (Laden et al. 2000). Short-term exposure to PM and traffic has been linked to a variety of acute physiological effects, including induction of oxidative stress, pulmonary and systemic inflammation, enhanced coagulability, endothelial dysfunction and autonomic dysfunction, all of which might be involved in triggering acute cardiovascular events (Peters et al. 2004, Brook & Rajagopalan 2007, Mills et al. 2007). Cardiovascular effects of long-term exposure to PM air pollution have been investigated in several large cohort studies, showing a consistent link between higher levels of ambient PM and cardiovascular disease (Brook et al. 2004, Miller et al. 2007). Some studies have also focused on traffic-related air pollution, using surrogate variables such as NO_2 or proximity to high traffic as exposure variables (Hoek et al. 2002, Finkelstein et al. 2004, Gehring et al. 2006, Hoffmann et al. 2006, Beelen et al. 2008).

Little is known about long-term mechanisms that lead to an increased risk of cardiovascular disease. Prior cohort studies have been limited to investigating the incidence of acute cardiovascular events, such as myocardial infarction, sudden cardiac death or stroke. Using

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ISSN 1354-750X print/ISSN 1366-5804 online © 2009 Informa UK Ltd
DOI: 10.1080/13547500902965096

cardiovascular events as the outcome, however, does not allow the distinction between triggering acute effects through short-term biological mechanisms in pre-existing disease from chronic effects on atherogenesis.

To investigate the influence of traffic exposure on atherogenesis, it is necessary to focus on subclinical markers of disease rather than acute events. Biological markers of the degree of atherosclerotic disease that can be used in large-scale epidemiological studies include the ankle-brachial index, the degree of coronary artery calcification and the carotid intima–media thickness.

Several recent studies have pointed to a possible involvement of long-term exposure to PM air pollution or high traffic in the development and progression of atherosclerosis, using different markers of subclinical atherosclerosis (Künzli et al. 2005, Erdogmus et al. 2006, Hoffmann et al. 2007, 2009, Diez Roux et al. 2008, Allen et al. 2009). In this article, current evidence linking long-term exposure to high traffic with coronary heart disease will be summarized, using recently published results from the Heinz Nixdorf Recall Study, an ongoing prospective cohort study in Germany (Schmermund et al. 2002, Hoffmann et al. 2006). Special focus is placed on the association of long-term residential traffic exposure with subclinical atherosclerosis, the major underlying pathology for cardiovascular disease.

Methods

Baseline data from the ongoing population-based, prospective Heinz Nixdorf Recall cohort study was used. The study design has been described in detail elsewhere (Schmermund et al. 2002). It was approved by the relevant institutional ethics committees and followed strict internal and external quality assurance protocols. The cohort comprises 4814 men and women aged 45–75 years from three large adjacent cities (Mülheim, Essen and Bochum) of the densely populated and highly industrialized Ruhr Area in Western Germany. The baseline assessment included a self-administered questionnaire and a personal interview regarding socio-demographic characteristics, lifestyle factors, medical history and current medications, physical examinations including anthropometric and blood pressure measurements, and comprehensive laboratory tests. Annual mean fine particulate air pollution exposure (year 2002) at the subjects' home addresses was estimated from the daily mean $PM_{2.5}$ concentration on a spatial scale of 5 km, derived from the EURAD dispersion and chemistry transport model (Memmesheimer et al. 2004).

To assess residential long-term traffic exposure on a small spatial scale, distances between residences and major roads (federal freeway and state highways with mean daily vehicle counts of 10 000–130 000) were calculated, using official digitized maps with a precision of at least ±0.5 m. The reference line for distance measurements was the median strip between traffic lanes. Distances were categorized as ≤10 m, 11–20 m, 21–30 m, 31–40 m, 41–50 m, 51–100 m, 101–150 m, 151–200 m and >200 m.

The clinical outcome variable was manifest coronary heart disease (CHD), defined as a self-reported history of a 'hard' coronary event like a myocardial infarction or a coronary intervention (application of a coronary stent, angioplasty, bypass surgery) at baseline. For the assessment of subclinical atherosclerosis, the degree of coronary artery calcification (CAC) and the ankle-brachial index (ABI) were used. CAC score, derived from non-contrast-enhanced EBCT (GE Imatron, South San Francisco, CA, USA), was determined using the method of Agatston et al. (1990).

ABI was calculated per leg as the ratio of the highest systolic brachial pressure, measured in the right and left arm, and the highest ankle artery pressure measured either in the posterior tibial or the dorsalis pedis artery, using a 8 MHz Doppler transducer (Kranzbühler, Logidop, Germany) (Kröger et al. 2006). Medical history of peripheral artery disease (PAD) was assessed by a standardized interview. A history of PAD was considered present if the subject could indicate precisely which kind of surgical or interventional procedures had been performed for PAD. All subjects with an ABI < 0.9 in one or both legs, and/or a history of prior PAD treatment were considered cases of PAD.

Crude and multiple adjusted logistic regression analysis was used for investigating the cross-sectional association of long-term residential traffic exposure with prevalence of CHD and PAD. Linear regression analysis was applied for examining associations of traffic exposure with the continuous subclinical measures of atherosclerosis (CAC and ABI). CAC was also dichotomized at the 75th age- and sex-specific percentile, which is a clinically used cut-off point for identifying high-risk patients, and analysed with logistic regression. Distance to high traffic was included in the analysis first as the natural logarithm of distances to take into account the exponential decline in concentration of traffic-related particles perpendicular to major roads (Zhu et al. 2002), and second in categories (0–50, 51–100, 101–200 and >200 m as reference category). Participants living more than 200 m away were assigned a value of 400 m, because traffic-related particle concentrations have usually reached background concentrations at that distance (Hitchins et al. 2000).

Results

Figure 1 illustrates the study region and the distribution of the 4814 participants' residences in relation to the

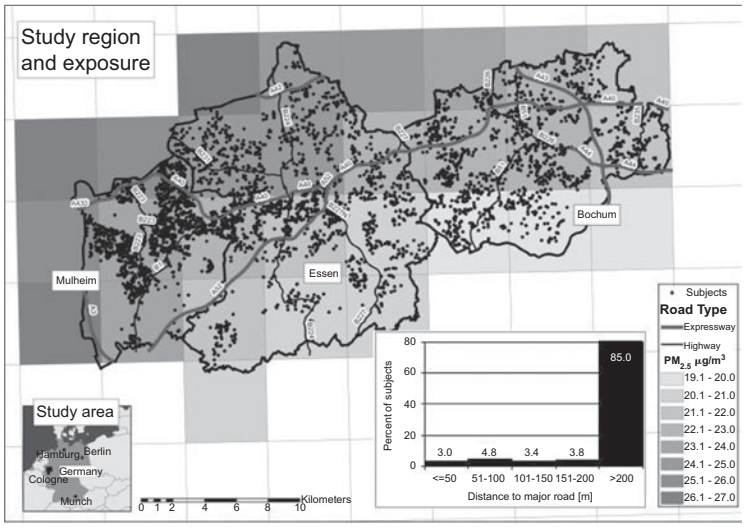

Figure 1. Study region and distribution of the 4814 participants' residences in relation to federal and state highways.

Table 1. Crude and adjusted estimated odds ratios (OR) for the association of high exposure to traffic emissions with prevalence of coronary heart disease ($n = 2596$) (Hoffmann et al. 2006).

Distance (m)	Participants, *n*	Cases, *n* (%)	Crude model		Adjusted model[a]	
			OR	95% CI	OR	95% CI
>200 (reference)	2596	187 (7.2)	1.0	–	1.0	–
>100–200	191	15 (7.9)	1.09	0.63–1.88	1.08	0.59–1.97
>50–100	143	16 (11.2)	1.55	0.91–2.66	1.71	0.92–3.16
≤50	79	10 (12.7)	1.76	0.99–3.45	1.55	0.71–3.42

[a]Adjusted for age, sex, educational attainment, history of hypertension, diabetes mellitus, HbA1c, low-density lipoprotein, high-density lipoprotein, triglycerides, BMI in five categories, waist-to-hip ratio, active smoking (regularly, occasionally), smoking history (time since quitting), environmental tobacco smoke at home, at work or in other places, city of residence, area of residence within city (north/south). CI, confidence interval.

distance to major roads. Most participants (85%) lived more than 200 m away from a major road; 3%, 5% and 8% of subjects lived within 50, 51–100 and 101–200 m, respectively. The mean annual $PM_{2.5}$ exposure was 22.8 µg m^{-3}, ranging from 19.8 to 26.8 µg m^{-3}.

Table 1 displays the crude and adjusted odds ratios for prevalence of CHD according to residential proximity to major roads. It shows an increase in the odds ratio for CHD in participants living closer to high traffic compared with those living more than 200 m away.

Table 2 shows the associations of chronic residential traffic exposure with CAC and ABI. For subjects living within 400 m of a major road, a reduction of the distance between residence and a major road by half is associated with a 7% increase in coronary calcification. Participants living within 50 m of a major road compared with those living more than 200 m away have 63% higher odds of having

Table 2. Estimated change (95% confidence interval (CI)) in coronary artery calcification (CAC) and the ankle-brachial index (ABI) associated with a reduction of the distance to a major road by half and odds ratio (OR, 95% CI) for high CAC, defined as a calcification score above the 75th age- and sex-specific percentile. Estimates for all participants with complete information on explanatory and outcome variables. Estimates for CAC are given as percent change and OR, for ABI as absolute change. Results published in Hoffmann et al. (2007, 2009).

	Change in CAC		Absolute change in ABI[a]	
	% change	95% CI	Absolute change	95% CI
Reduction of distance by 50%				
Unadjusted model for distance	10.2	1.7–19.4	−0.007	−0.011 to −0.003
Fully adjusted model for distance[b]	7.0	0.1–14.4	−0.005	−0.009 to −0.001
	Adjusted OR for high CAC (75th age and sex-specific percentile)			
	OR	95% CI	Absolute change	95% CI
Distance categories (m)				
>200	1.00	–	0.0	–
101–200	1.08	0.85–1.39	−0.015	−0.030 to 0.0
51–100	1.34	1.00–1.79	−0.002	−0.021 to 0.016
≤50	1.63	1.14–2.33	−0.024	−0.047 to −0.001

[a]Participants with an ABI > 1.3, indicating medial sclerosis, are excluded from the linear regression analysis. [b]The fully adjusted model includes the following covariates: annual $PM_{2.5}$, city and area of residence, age, sex, education, smoking variables, environmental tobacco smoke, physical inactivity, waist-hip ratio, diabetes, blood pressure, lipid status.

a high amount of CAC. ABI is also associated with proximity to major roads; however no clear exposure–response relation can be observed in the complete study group.

Discussion

Earlier work has shown that long-term exposure to PM leads to increased cardiovascular morbidity and mortality (Brook et al. 2004). Traffic-related PM, in particular, has received great interest lately, because it is one of the major components of urban air pollution and has been shown to exert acute effects on the vasculature (Mills et al. 2005, Törnqvist et al. 2007, Peretz et al. 2008). Using baseline data from the population-based prospective Heinz Nixdorf Recall Study, we showed that living close to a heavily trafficked road is not only associated with prevalence of coronary heart disease, but also with the degree of subclinical atherosclerosis, the major underlying pathology for cardiovascular disease. This provides a possible link for the observed cardiovascular health effects of long-term exposure to PM. Biological plausibility for a causal relationship between air pollution and atherosclerosis is supplied by animal studies (Sun et al. 2005). Our results are also supported by epidemiological findings showing associations of long-term residential exposure to PM with the carotid intima–media thickness, a measure of general atherosclerosis (Künzli et al. 2005, Diez Roux et al. 2008). However, other investigators did not find consistent associations of long-term exposure to traffic or PM with other measures of subclinical atherosclerosis (Allen et al.2009, Diez Roux et al. 2008). Different methods in the assessment of long-term traffic and PM exposure and in PM composition across study areas could have contributed to these differences between studies.

Motor vehicle traffic is a major source of intra-urban submicrometer particles. These might have a higher toxicity than larger particles due to their small size and greater surface area, facilitating the binding of toxic components such as transition metals. Noise is another pathogenic component of traffic-related emissions, which could explain part of the observed association. Living close to highly trafficked roads is also associated with low individual as well as neighbourhood socioeconomic status (SES), both of which have been shown to be associated with cardiovascular disease. These effects, however, were independent from the associations with traffic proximity (Dragano et al. 2007).

When investigating the effect of residential traffic exposure, small-scale distance measurements are necessary to identify highly exposed individuals. In the Heinz Nixdorf Recall Study, a high precision of distance measurements, availability of traffic density data, and a relatively homogenous $PM_{2.5}$ urban background concentration throughout the study region facilitated the identification of independent traffic-related effects.

Personal exposure to traffic is also determined by daily activities and working conditions. Future studies on the effect of traffic exposure should incorporate information on time spent in various microenvironments, including time spent in traffic.

Atherosclerosis and coronary heart disease take a long time to develop; therefore exposures 10–15 years before the assessment of (sub)clinical disease are more relevant than exposures taken concurrently. Epidemiological studies so far are based primarily on cross-sectional analyses and assume that the current traffic exposure contrast within the study population has not changed substantially. This might not hold true, however, because participants might have relocated several times before the onset of the study. Future studies should incorporate the residential history of participants for the assessment of the relevant exposure.

In summary, this review presents current evidence on the association of residential exposure to highly trafficked roads with coronary heart disease and measures of subclinical atherosclerosis, using data from a population-based study in Germany. Considering the continuing rise in motorized vehicle usage and the important role of atherosclerosis in morbidity and mortality, these findings have high public health relevance and should be corroborated in prospective studies.

Acknowledgements

We thank the investigative group and the study staff of the Heinz Nixdorf Recall Study. We also wish to thank the Landesamt für Natur, Umwelt und Verbraucherschutz NRW for providing the data from the EURAD air quality model. We thank the Heinz Nixdorf Foundation (Chairman: Dr jur. G. Schmidt), the German Ministry of Education and Science, the German Research Foundation (DFG; Project SI 236/8-1 and SI236/9-1) and Sarstedt AG & Co. for the support of the study.

***Declaration of interest*:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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