Cardiovascular Effects of Air Pollution: What to Measure in ECG?

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Epidemiologic evidence indicates that air pollution adversely affects the cardiovascular system, leading to increased cardiovascular morbidity and mortality. However, the mechanisms of such an association are unknown. Although potential mechanisms of deleterious effects of air pollution may involve response of the respiratory system, immunologic response, or coagulation abnormalities, the cardiovascular system seems to be the common end point of these pathways. Cardiovascular response to any stress (which may include air pollution) is a consequence of a complex interplay between the autonomic nervous system governing centrally mediated control of the cardiovascular system, a myocardial substrate (current state of the myocardium) altered in the course of disease processes, and myocardial vulnerability leading to arrhythmogenic or ischemic response. Through the use of standard electrocardiograms (ECGs), exercise ECG testing, and long-term ambulatory ECG monitoring, modern electrocardiology makes a valuable contribution to understanding the different mechanistic factors involved in the increase in adverse cardiovascular events due to air pollution. Heart rate variability analysis can provide quantitative insight into the autonomic response of the cardiovascular system to air pollution. Analysis of ventricular repolarization in an ECG (both duration and morphology) gives valuable information about the status and dynamic behavior of myocardium, reflecting myocardial substrate and vulnerability. ST-segment analysis of ECGs is used routinely to monitor the magnitude of ischemia and could be used to monitor subtle changes in the myocardium in subjects exposed to air pollution. Comprehensive analysis of ECG parameters describing the influence of the autonomic nervous system, the role of myocardial substrate, and the contribution of myocardial vulnerability could and should be employed in air pollution studies, especially as those mechanistic components have been proven to contribute to increased cardiovascular morbidity and mortality in general. *Key words*: air pollution, cardiac death, cardiovascular morbidity, ECG, electrocardiogram, heart rate variability, particulate matter, repolarization. — *Environ Health Perspect* 109(suppl 4):533–538 (2001).
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The London fog incident in 1952 demonstrated that air pollution is associated with an abrupt increase in mortality (*1*). Although levels of air pollution have been greatly reduced since the 1950s, it has been estimated that as many as 60,000 deaths each year in the United States are related to air pollution (*2*,*3*). Among the components of air pollution, fine particles, which have a mass median aerodynamic diameter less than 10 μm (PM_{10}) and are emitted mainly from the combustion of fossil fuels, have been shown epidemiologically to be associated with mortality (*4*). PM_{10} may be deleterious because it consists of a mixture of toxic compounds such as soot, acid condensates, and sulfate and nitrate particles, and because of its small diameter, allowing for inhaled PM_{10} to penetrate deeply into the lung (*5*). Increased levels of air pollution are associated with death not only from lung cancer but also from cardiopulmonary disease (*4*). The influence of air pollution on cardiovascular diseases is of growing concern. Increased mortality attributed to air pollution could be caused by particulate matter alone or, more likely, in combination with other pollutants such as carbon monoxide (CO) or nitrogen dioxide (NO_2). Air pollution that was monitored in Phoenix, Arizona, from 1995 to 1997comprised a mixture of PM_{10}, particles with a mass median aerodynamic diameter less than 2.5 μm ($PM_{2.5}$), and CO, NO_2, sulfur dioxide (SO_2), and ozone (O_3) and was found to be associated with increased cardiovascular mortality (*6*). Cardiovascular morbidity is also affected by air pollution, as demonstrated by Linn et al. (*7*) in the Los Angeles, California, area from 1992 to 1995 where PM_{10}, CO, and NO_2 were found to have a significant association with cardiovascular hospitalizations. Schwartz (*8*) reported that daily variations of PM_{10} and CO were linked to daily hospital admissions among the elderly. Knöbel et al. (*9*) showed that the rate of sudden infant death syndrome increased with elevated levels of air pollution. More direct evidence of a relationship between fatal cardiac arrhythmia and air pollution was presented recently by Peters et al. (*10*). They surveyed episodes of defibrillation by implanted cardioverter defibrillators as related to daily air pollution in the Boston, Massachusetts, area. They found that frequency of defibrillator discharges showed a significant correlation with increased levels of NO_2 and black carbon, and to a lesser extent with CO and PM_{10}, suggesting that air pollution is a risk factor for cardiovascular diseases and for arrhythmic events in particular (*10*). In that study cardiac arrhythmias often occurred 2 days after incidences of increased air pollution. Watkinson et al. (*11*) used an animal model of pulmonary hypertension to demonstrate that the incidence and duration of cardiac arrhythmias were increased by raising the dose of inhaled small particles in pulmonary hypertensive rats but not in normal rats. The above observations suggest that the effect of air pollution on the cardiovascular system depends to a major extent on the condition of ventricular myocardium (myocardial substrate), i.e., the presence of underlying heart disease predisposes animals to air pollution–related changes in the cardiovascular system.

The mechanisms by which air pollution affects the cardiovascular system are unknown, although several possible mechanisms have been suggested including the neural mechanisms related to the response of the autonomic nervous system through direct reflexes from airways or through inflammatory response; the chemical effect on ion channel function in the myocardial cell; ischemic response in the myocardium; and the inflammatory response that triggers endothelial dysfunction, atherosclerosis, and thrombosis.

It is worth emphasizing that cardiovascular responses to air pollution do not occur in isolation from other systems, which seems to contribute to this response. Most current studies are designed to simultaneously study parameters describing cardiac response [such as electrocardiogram (ECG) signals], lung function, immunologic response, or specific blood variables. Such a comprehensive approach can provide insight into overall mechanisms underlying biologic effects of air pollution on the human body.

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We are pleased to have the opportunity to contribute our ECG-related research projects conducted by M. Utell, M. Frampton, and G. Oberdoerster from University of Rochester Medical Center, Rochester, New York, USA; H. Gong from Rancho Los Amigos Medical Center, Downey, California, USA; and A. Peters and E. Wichmann from GSF Forschungszentrum GmbH, Neuherberg, Germany.

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Pathomechanisms of Cardiac Death

Although the influence of air pollution on the cardiovascular system is being identified in epidemiologic studies, the pathophysiologic mechanism underlying this association is not known. Cardiac death is a consequence of a complex interplay between the autonomic nervous system governing centrally mediated control of the cardiovascular system, a myocardial substrate (current state of the myocardium) altered in the course of disease processes, and myocardial vulnerability leading to arrhythmogenic or ischemic response (Figure 1). The presence of a single such condition is usually not sufficient to trigger death. For example, sympathetic activation in a subject with a healthy heart is not likely to lead to life-threatening arrhythmias. Usually a biologic or psychologic stress induces a cascade of events by increasing sympathetic activation, which may alter the myocardial substrate and subsequently increase myocardial vulnerability, leading to ventricular tachyarrhythmias, aggravation of ischemia, or heart failure and death. Air pollution may be a stressor sufficient to trigger this chain of events, especially in vulnerable subjects such as the elderly, patients with heart failure, or those with chronic obstructive pulmonary disease (COPD). Noninvasive electrocardiology provides an opportunity to measure and monitor ECG parameters reflecting the key components of the "cardiac death triangle." Several of these parameters have been used to identify high-risk individuals in studies focused on risk stratification of patients after myocardial infarction, those with cardiomyopathy or hypertension (*12*). Monitoring these ECG parameters might identify cardiovascular factors contributing to increased risk of cardiac death in response to air pollution.

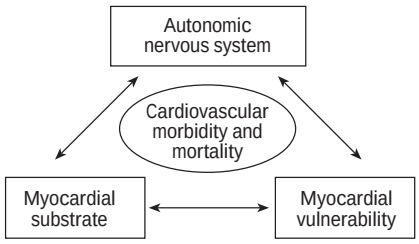

Figure 1. Factors contributing to cardiac morbidity and mortality. Specific ECG parameters reflecting those factors are listed in Table 1.

Table 1. Noninvasive ECG parameters describing biologic phenomena contributing to increased risk of cardiac death.

Autonomic nervous system
Heart rate variability
Time-domain (SDNN, rMSSD, pNN50, SDANN, SDNNIX)
Frequency-domain (TP, ULF, VLF, LF, HF, LF/HF ratio)
Myocardial substrate
Left ventricular hypertrophy (QRS voltage, QRS product)
QRS duration and morphology (conduction disturbances, pathologic Q waves)
Late potentials
QT interval duration
QT dispersion
Principal component analysis of T wave
Exercise-induced ST-segment changes
Myocardial vulnerability
Frequency and complexity of ventricular arrhythmias
ST-segment changes
QT–RR relationship
QT- and T-wave variability
T-wave alternans

The cardiovascular mechanisms leading to cardiac death, sudden cardiac death, and increased cardiovascular morbidity are very similar. ECG parameters described below provide comprehensive information about the mechanisms underlying increased risk of cardiovascular morbidity and mortality. Cardiac arrhythmias, especially atrial fibrillation and supraventricular arrhythmias, are the leading cause of hospital admissions for cardiovascular causes in the United States and they frequently are clinical manifestation of underlying cardiovascular disorders including ischemic heart disease and congestive heart failure. ECG parameters describing myocardial damage (abnormal QRS complex or T-wave morphology) or myocardial ischemia (ST–T-wave changes) give information about the presence and the magnitude of myocardial involvement underlying increased risk of cardiovascular morbidity and mortality. Monitoring these parameters in conditions of spontaneous (ambient) or experimental air pollution in high-risk patients is likely to elucidate mechanisms by which air pollution may affect the cardiovascular system.

Physiologic and Methodologic Aspects of Heart Rate Variability

The concept that air pollution–related increases in cardiac mortality and morbidity may operate through changes in autonomic control of the heart leads to recent interest in studies employing heart rate variability (HRV) analysis (*13,14*). Heart rate and the entire cardiovascular system remain under the constant influence of both sympathetic and parasympathetic innervation from the autonomic nervous system. Parasympathetic effect is conveyed through vagal nerves originating in the central nervous system (dorsal motor nucleus and nucleus ambiguus) and innervating sinus node, atrio-ventricular node, atrial and likely also the ventricular myocardium. Sympathetic nerves originate in the upper thoracic region of the spinal cord and postganglionic fibers innervate the sinus node, the atrio-ventricular node, and the atrial and ventricular myocardium. An increase in parasympathetic activity slows the heart rate, whereas an increase in sympathetic activity increases the heart rate by directly affecting the sinus node. Both vagal and sympathetic fibers may carry afferent impulses from the heart to the brain, triggering a feedback response from the autonomic nervous system.

The intrinsic heart rate, governed by electrical function of the sinus node in the heart, is 100–120 beats per minute. However, the parasympathetic system has profound influence on the sinus node and overdominates the influence of the sympathetic system, which contributes to normal resting heart rates of 55–70 beats per minute. In cases of stress (such as exercise), there is an increase in sympathetic discharges from the autonomic nervous system, which leading to an increased heart rate. Various cardiac conditions (e.g., myocardial infarction, hypertension) and noncardiac disorders (e.g., diabetes, COPD) are associated with altered autonomic function of the cardiovascular system caused by increased sympathetic activation, withdrawal of parasympathetic tone, or both.

Heart rate provides indirect insight into constant interplay between the sympathetic and parasympathetic systems and therefore monitoring changes in heart rate (i.e., heart rate variability) is useful in determining the effect of the autonomic system on the heart (*12–15*). Frequent changes in heart rate occur in response to respiration (12–15 cycles per minute depending on respiratory rate); other changes in heart rate are of slower periodicity and may occur in cycles of 1 every 10 sec up to 1 every few minutes. Heart rate is measured by ECG using the duration of the RR interval (i.e., the interval between R peaks of two consecutive QRS complexes representing heart beats), and beat-to-beat variations in the RR interval duration reflect changes in the autonomic nervous activity. Because the analysis of the RR interval variation includes only so-called normal beats, i.e., beats originating in the sinus node (atrial and ventricular ectopic beats are excluded), the term NN intervals (normal-to-normal beat intervals) is used to emphasize this aspect of the technique. Variation in the NN interval duration can be measured using several methods; time-domain statistical measures of variability and frequency-domain analysis of the power spectrum of the heart rate are the most popular approaches. As indicated above, a prolonged ECG recording (at least 5–10 min but usually 24 hr) is needed to obtain full insight into the periodicity of heart rate changes. The standard 12-lead ECG with 10-sec recording is too short and cannot be used to determine HRV. Instead, long-term Holter recordings became the standard method to obtain information about beat-to-beat changes in heart rate.

Time-Domain HRV Analysis

The time-domain HRV approach is based on statistical analyses of the NN interval variation (*12–14*). Classical parameters are SDNN (standard deviation of normal-to-normal sinus beat intervals); rRMSSD (root mean square of successive differences in NN intervals); and pNN50 (percent of adjacent NN intervals differing by more than 50 ms). All three parameters mainly reflect the influence of the parasympathetic system on the heart, and they highly correlate with each other. Additional time-domain parameters (SDANN and SDNNIX) are less frequently used, especially as their physiologic meaning is less well understood. Figure 2 shows examples of NN interval distribution in subjects with normal and decreased HRV. Time-domain HRV parameters are stable over time and show good reproducibility, which makes them useful in clinical studies and in research applications. SDNN, representing overall variability of heart rate, has been shown to be a predictor of cardiac death in various patient populations, including patients with myocardial infarction, nonischemic cardiomyopathy, hypertension, diabetes, COPD, and even in healthy subjects (*12–15*).

Frequency-Domain HRV Analysis

The frequency-domain approach is based on the power spectral analysis of the NN interval series (tachogram) for identification of periodic components in the ECG signal and estimation of their amplitude and frequency (*12–14*). Respiratory modulation of the heart rate is driven by the number of breaths per minute, usually 12–15 in a healthy adult subject; the number could be expressed as 12–15 cycles per 60 sec, i.e., 0.20–0.25 Hz. This frequency is in the high frequency (HF) band of HRV, which is defined between 0.15–0.40 Hz, reflecting respiratory modulations of 9–24 breaths per minute. The ECG signal consists of several components apart from respiratory (vagally) modulated HF, and frequency-domain HRV analysis provides information about the contribution of all frequencies representing oscillatory patterns of heart rate. Figure 3 compares power spectrums of heart rate in a normal subject and in a subject with depressed HRV. The energy (magnitude) of the overall variability is measured for the entire spectrum, i.e., total power (TP) from 0 to 0.40 Hz, which is mathematically equal to heart period variance $[SDNN]^2$. The energy of HRV is also measured in specific frequency bands defined as HF (0.15–0.40 Hz), low frequency (LF; 0.04–0.15 Hz), very low frequency (VLF; 0.003–0.04 Hz), and ultra-low frequency (ULF; < 0.003 Hz). The total power usually is calculated as the sum of the above components of the spectrum between 0 and 0.4 Hz, reflecting the total HRV. As described above, the HF represents parasympathetic (respiratory) modulation of the heart. The LF power reflects modulation of sympathetic and parasympathetic tone but with strong dominance of sympathetic influence; therefore LF is considered an indicator of sympathetic tone and baroreflex sensitivity (*13*). Physiologic background of VLF and ULF is not well understood; they account for long-term regulation mechanisms (< 0.04 Hz, i.e., 1 cycle every 25 sec up to 1 cycle every few minutes), and they are believed to reflect thermoregulation and possibly the renin–angiotensin system (*13*). Because the heart is affected by sympathovagal modulation, the frequency-domain method provides the opportunity to evaluate the relative contribution of sympathetic and parasympathetic tones by computing the LF/HF ratio (sympathovagal tone). Frequency-domain HRV measures are less stable and less reproducible than time-domain HRV parameters, especially if used for analysis of short-term ECG recordings. There is large natural physiologic variation of frequency-domain values. In short-term recordings, frequency-domain analysis yields reproducible results, assuming reproducibility of recording conditions. Time- and frequency-domain parameters computed from 24-hr recordings correlate well with each other (*13*). Frequency-domain parameters, including HF, LF, LF/HF ratio, VLF, and ULF, can be used to identify patients at risk for cardiac death (*12–14*).

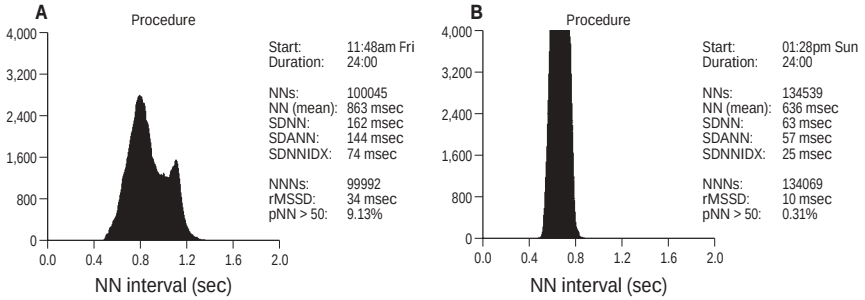

Figure 2. Time-domain HRV analysis: distribution of NN intervals in a healthy subject (*A*) and in a patient with dilated cardiomyopathy (*B*). Respective SDNN values are 162 msec and 63 msec, and respective rMSSD values are 34 msec and 10 msec.

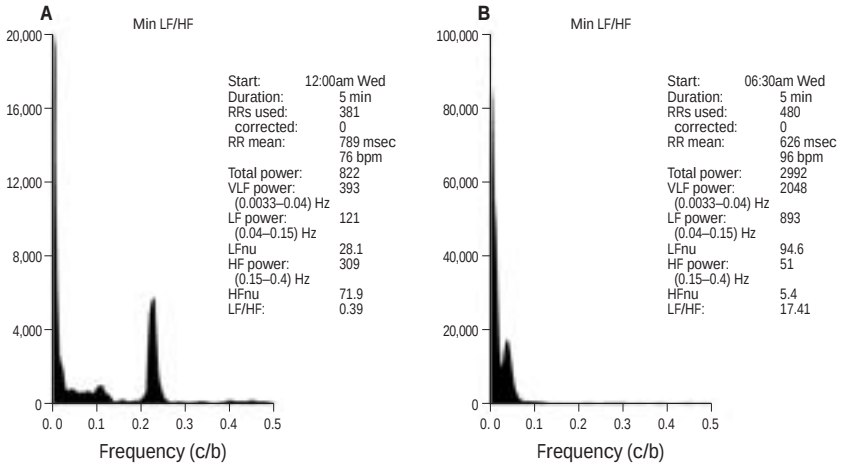

Figure 3. Frequency-domain HRV analysis: distribution of NN intervals in a healthy subject (*A*) and in a patient after myocardial infarction (*B*). c/b, cycles per beat. HFnu, high frequency content normalized for total power; LFnu, low frequency content normalized for total power. In healthy subject, LF = 121 $msec^2$, HF = 309 $msec^2$, and LF/HF ratio = 0.39. In patient after myocardial infarction, LF = 893 $msec^2$, HF = 51 $msec^2$, and LF/HF ratio = 17.40.

Heart Rate Variability and Air Pollution

Regardless the method used to quantify HRV, decreased HRV implies impaired autonomic nervous activity and increased risk for cardiac events associated with imbalance between effects of sympathetic and parasympathetic systems on the cardiovascular system (*12–15*). Data in the literature are still limited describing the association between air pollution and changes in HRV; nevertheless, they indicate that in some patient populations (or in some pathologic conditions in animal laboratories) air pollution may contribute to altered HRV. Pope et al. (*16*) measured HRV parameters and levels of PM_{10} and found that elevation of

PM_{10} was associated with increased heart rate and decreased HRV. Although the study had some limitations (a small number of subjects with various diseases and medication), results suggested that modulation of autonomic nervous activity was one of the mechanisms by which air pollution affected the cardiovascular system (*16,17*). Recently, Gold et al. (*17*) further confirmed that changes in HRV parameters were induced by air pollution in a study of elderly residents in a Boston housing community. The authors measured daily variations of HRV parameters and levels of air pollution and showed that increased levels of $PM_{2.5}$ correlated significantly with decreased HRV (*17*). Animal studies also indicate that concentrated ambient particles induce HRV changes consistent with increased sympathetic nervous system activity (*18,19*). However, questions remain about the mechanisms linking inhalation of ambient particles and HRV: Are HRV parameters changed because of airway-mediated reflexes from the autonomic nervous system? Is the response of the autonomic nervous system secondary to the direct effect of particles inducing inflammatory response? Does particle-triggered ischemia play a role?

Myocardial Substrate

The pathophysiology of cardiac death indicates the important role of changes in the myocardium that create the substrate for mechanisms leading to increased morbidity and frequently to fatal cardiac events (*13*). Changes in myocardial substrate are routinely detected by evaluating hemodynamic function of the heart (using echocardiography, radionuclide, or angiographic methods) and by analyzing features of electrical activity in the myocardium using electrocardiography methods. Myocardial infarction, chronic ischemic heart disease, hypertension, and COPD may lead to significant changes in myocardium expressed in ECG recordings as signs of myocardial injury, abnormal rhythm, abnormal conduction, ischemia, or hypertrophy. An ECG signal provides useful information about the myocardial substrate (Figure 4), with P waves representing atrial activation (depolarization), PR intervals reflecting atrio-ventricular conduction of electrical signals between sinus node and ventricular endocardium, QRS complexes representing ventricular activation (depolarization), and QT intervals, ST segments, and T waves describing specific aspects of ventricular deactivation (repolarization). ECG analysis of parameters reflecting myocardial substrate is critical to integral evaluation of mechanisms contributing to increased morbidity and mortality (*12,13*).

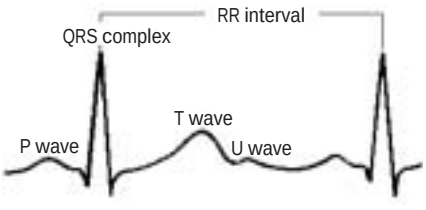

Figure 4. Schematic presentation of ECG curve with identification of specific waves.

QRS Complex

Chronic ischemic processes, hypertension, COPD, or even asthma may induce myocardial changes affecting both ventricular depolarization and repolarization. Changes in the ventricular depolarization process (frequently caused by myocardial fibrosis) can be assessed by evaluating duration and morphology of the QRS complex in standard and in signal-averaged ECGs (*20*). Detection of QRS prolongation, late potentials, or fractionation of the QRS complex may identify individuals with increased propensities to arrhythmogenic response to air pollution. Although one may speculate that air pollution could affect myocardial depolarization, it is difficult to imagine that changes would be large enough to be detectable by monitoring QRS changes.

Myocardial Ischemia (ST-Segment Analysis)

Chronic myocardial ischemia is a silent risk factor, creating suitable conditions for increased vulnerability to arrhythmias and increased risk of heart failure (*21*). Standard exercise testing with ST-segment monitoring or 24-hr Holter ST-segment monitoring may provide insight into the magnitude of ischemic myocardial changes. Although 1-mm ST depression is a clinically used parameter for detecting ischemic response, it is possible that air pollution could induce ischemic changes of lesser degree in patients with ischemic heart disease. Heart rate adjustment for ST-segment analysis may be of further benefit in detecting more subtle changes in the ischemic milieu of the myocardium.

QT Interval—Ventricular Repolarization

Ventricular repolarization is a complex process with a proven critical role in the arrhythmogenic response. A multitude of ion currents operating during repolarization makes this period vulnerable to even subtle changes in autonomic tone, oxygenation of myocardial cells, or electrolyte changes. The paradigm of long QT syndrome, an inheritable disorder of prolongation of ventricular repolarization (QT interval) and a propensity toward life-threatening ventricular arrhythmias, continuously improves our understanding of the electrophysiology of repolarization processes in the myocardial cell (*22,23*). Duration of the QT interval, adjusted for heart rate (QTc), is widely used in clinical medicine to quantify baseline repolarization abnormalities as well as to identify changes in repolarization duration due to additional factors such as medications. It is possible that air pollution may alter repolarization, leading to prolonged repolarization throughout mechanisms operating on potassium or calcium ion channels. Heterogeneity of repolarization in the myocardium has been found to be an important substrate for ventricular arrhythmias (*24,25*). The magnitude of repolarization heterogeneity could be estimated by quantifying T-wave morphology (for example, using principal component analysis). Analysis of QT dispersion is less important, as there is no proof that this ECG parameter reflects repolarization heterogeneity and as QT dispersion is, to a major extent, an indirect and inaccurate description of T-wave (T-loop) morphology (*26,27*). Current approaches quantifying repolarization morphology seek methods independent from T-wave end point location and that quantify the overall shape of the repolarization segment. Subjects with underlying increased dispersion of refractoriness, in the course of ischemic heart disease, cardiomyopathy, genetic predisposition (i.e., long QT syndrome, ion channel gene or beta-receptor gene polymorphisms), or in the course of COPD, could be prone to arrhythmias triggered by air pollution. For example, Sarubbi et al. (*28*) found that QTc dispersion was significantly greater in patients with severe COPD than in healthy subjects. It is also possible that subtle changes in ion channel function could be triggered by the indirect influence of air pollution through autonomic changes, ischemic, or inflammatory processes. However, to date there has been no experimental or clinical evidence for an association between air pollution and repolarization abnormalities.

Myocardial Vulnerability

The myocardium is under the constant influence of internal and external stimuli, which contributes to the dynamic behavior of many of the previously described ECG parameters. Some individuals might be more likely to adverse outcomes because of myocardial vulnerability that predisposes them to arrhythmic or ischemic events. Myocardial vulnerability could be evaluated using ECG monitoring methods by quantifying cardiac arrhythmias, transient ischemia, or dynamic behavior of repolarization (*12,13*). Presence of a myocardial substrate (e.g., an old myocardial infarction) alone rarely leads to an adverse outcome. Adverse outcomes in such postinfarction patients usually are caused by new occurrences of myocardial ischemia or cardiac arrhythmias. It is conceivable that air pollution may increase myocardial vulnerability by

triggering cardiac arrhythmias, aggravating myocardial ischemia, or altering the dynamics of cardiac repolarization. Therefore, long-term Holter ECG monitoring is likely to provide information about the effects of air pollution on those measures of myocardial vulnerability. Clear support for the importance of myocardial vulnerability in air pollution studies has been provided by recent analysis of patients with implantable cardioverter-defibrillators, where an increase in air pollution was associated with more frequent arrhythmic events. Measuring frequency and complexity of cardiac arrhythmias in long-term ECG recording might serve as a noninvasive parameter describing myocardial vulnerability in air pollution studies. Similarly, monitoring ST segments by ECG might help identify a potential link between air pollution and transient myocardial ischemia with more ischemic episodes present during periods of increased air pollution. Also, changes in ventricular repolarization might be also present only when monitoring dynamic features of repolarization, such as QT adaptation to changing heart rates, QT- and T-wave variability, or T-wave alternans (*12*,*13*,*29*–*31*). Figure 5 illustrates changes in repolarization dynamics presented as a slope of the association between repolarization duration and heart rate and as beat-to-beat changes in repolarization duration. Computerized ECG analysis of repolarization duration and morphology may yield information about the potential contribution of static and dynamic repolarization abnormalities in air pollution–related vulnerability to ventricular arrhythmias and sudden cardiac death (*12*,*27*).

Rochester ECG Core Lab Experience

The above concepts of ECG monitoring for air pollution studies are based on our ongoing experience acquired during various cardiovascular projects identifying parameters improving risk stratification in high-risk cardiac patients. More important, these concepts are based on our ongoing involvement in several air pollution studies conducted by our numerous collaborators in experimental settings (rats exposed to air pollution), in clinical studies (healthy subjects and subjects with asthma or COPD exposed to controlled levels of air pollution), and in epidemiologic studies (postinfarction patients exposed to spontaneous environmental air pollution). This growing experience and increasing amounts of data will help us determine the ECG markers most useful in identifying risk for individuals affected by air pollution.

Summary

In conclusion, although evidence that air pollution affects the cardiovascular system is growing, the mechanisms of such an association are unknown. Modern electrocardiology can offer a broad spectrum of measures that identify the contribution of different mechanistic factors to the air pollution–related increase in cardiovascular adverse outcomes. Comprehensive analysis of ECG parameters describing the influence of the autonomic nervous system, the role of the myocardial substrate, and the contribution of myocardial vulnerability should be conducted in air pollution studies, especially because those mechanistic components have been proven to contribute to increased cardiovascular morbidity and mortality in general. Our recommendations for ECG analysis in air pollution studies include evaluating the following parameters obtained from long-term Holter recordings: SDNN and LF/HF ratio (reflecting the influence of the autonomic nervous system on the heart), QT duration and T-wave morphology (reflecting changes in the myocardial substrate), and cardiac arrhythmias, ST-segment, and QT dynamics analyses (reflecting various aspects of myocardial vulnerability). Current computerized ECG technology permits conducting such analyses at experimental, clinical, and epidemiologic levels.

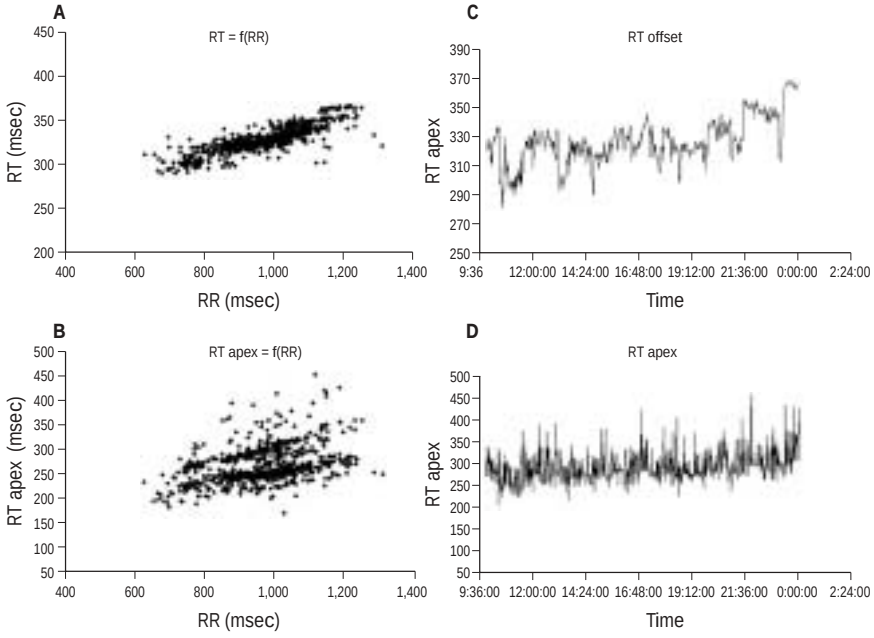

Figure 5. Examples of graphs illustrating dynamic behavior of repolarization measured from R-wave peak to T-wave end (RT offset) and from R-wave peak to T-wave peak (RT apex). (*A*) relationship between RT offset and RR interval. (*B*) Relationship between RT apex and RR interval. (*C*) Beat-to-beat variability of RT offset interval over time. (*D*) Beat-to-beat variability of RT apex interval over time.

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