were presented at the spring meetings of the Society of Toxicology and Experimental Biology 1994 and have been submitted for publication.

Arthur Penn, PhD
Carroll Snyder, PhD
Institute of Environmental Medicine
Anthony J. Lanza Research Laboratories
Tuxedo, New York

References

Aberrant Ventricular Conduction and Ventricular Ectopy

The recent contribution by Suyama et al1 attests to their continuing interest in the differentiation between aberrant ventricular conduction and ventricular ectopy in patients with atrial fibrillation. These workers have previously used plotting of RR intervals from Holter ECG recordings in patients with atrial fibrillation and of ECG data from a canine model of simulated arrhythmia.2,3 In this latest communication, they provide along with RR interval scattergrams from continuous ECG recordings unequivocal characterization of the nature of widened QRS complexes obtained by intracardiac electrophysiological procedures. I have some remarks and requests for clarification that do not detract from my belief that this is an important scientific communication.

The authors set the stage of their argument in their introduction by stating that differentiation between aberrant ventricular conduction and ventricular ectopy has etiologic, prognostic, and therapeutic (presumably independent of other factors) importance, without citing any relevant literature. I am not aware of any previous work supporting such a thesis, particularly for patients with atrial fibrillation, who are the focus of their study. Seven of the authors’ group 1 patients with chronic atrial fibrillation had only aberrant ventricular conduction and 6 patients in the same group had only ventricular ectopy. Was there any difference in the etiologic, prognostic, or therapeutic correlates in these two sets of patients, the small sample sizes not withstanding? To partially counteract this sample limitation, the authors could address this question by using data from their group 2 patients who did not have electrophysiologically validated their arrhythmia; again, the 16 patients with only aberrant beats and the 11 with only QRS complexes of ventricular origin with chronic atrial fibrillation could be compared. On the other hand, if the introductory comment of the authors refers to patients in sinus rhythm, generalization to other rhythms constitutes an inappropriate extrapolation. Furthermore, in either case, relevant literature should have been cited.

(CO) levels. The reasons for this are not intuitively obvious. Being a gas, CO readily diffuses through air and in a closed system will eventually reach a steady state. In contrast, TSP, which precipitates on standing and is adsorbed by carpets, clothing, drapes, etc., are not likely to reach a steady state. Thus, when sampling TSP levels, distance from the smoking source and time elapsed after the source is extinguished must be considered. This is especially important in “field” measurements. In contrast, CO levels are relatively unaffected by these factors and would appear to be better surrogates for integrated SS smoke concentrations.

Based on our published TSP values, Coggins characterizes our exposure concentrations as “massive” and claims that our TSP levels are 300-fold greater than those found in the homes of smokers. However, published levels of TSP in offices, restaurants, and so on vary by more than an order of magnitude (see Chapter 6 in Coggins’ Reference 5), and if the higher concentrations are used for reference, our TSP concentration is only 20 times that reported in public places. Clearly, these values are still high. However, if, instead of TSP, CO is used as a surrogate for SS smoke, then our exposure levels are only about twice as high as those found in some public places where smoking is permitted (see Appendix 3 in Coggins’ Reference 5).4

Coggins states that our vascular results are at variance with those from a study conducted at his laboratory (Reference 3 in Coggins’ letter). Our study differs in two significant ways from the study conducted by Coggins et al.1 First and most important, rats were used in that study. It is well known that rats are notoriously poor models for studying arteriosclerotic plaque development. In male Sprague-Dawley rats (the strain used by Coggins et al), even at 24 months of age only 1 of 392 rats displayed signs of arteriosclerosis.5 Before 52 weeks of age, no arteriosclerosis was detected. In their study, the oldest rats were killed at ~20 weeks of age. Thus, the absence of arteriosclerosis in these animals is not unexpected. In contrast, and as stated in our introduction, we chose cockerels because, like humans, they are susceptible to plaque development and because the abdominal aorta plaques in cockerels are morphologically and ultrastructurally similar to human coronary artery plaques.6-8 Second, Coggins et al make no mention of attempts to quantify plaque development. They state only that histopathological examinations were performed on aorta samples. In contrast, we quantified plaque development using digitized images of the plaques present in the aortic cross-sections. It is noteworthy that Coggins et al conclude that “ETS is unlikely to have any (emphasis added) significant toxicological activity in humans” based on the results of a study employing both a wholly inappropriate animal model and a nonquantitative analysis of plaque development.

Coggins mistakenly states that our exposures were conducted with freshly generated SS smoke and not with aged and diluted SS smoke. He also mistakenly states that we made “extensive” modifications to our commercial cigarette smoke generator. Our “Methods” section clearly states that the smoke-generating chamber was connected via 2-inch (diameter) pipe to the 4 adjacent exposure chambers and that air flow in each exposure chamber was regulated at 300 L/min. One can imagine the aging and dilution that occurs when air at 1200 L/min carries the SS smoke from 5 lighted cigarettes into 4 separate exposure chambers. We also clearly stated the puff characteristics employed in generating the SS smoke (a 30-ml, 2-second puff per cigarette, 4 times/min). These puff characteristics generated relative TSP and CO levels comparable to those reported by Coggins et al (his Reference 3).1
For example, at the highest concentration they used, the CO (ppm)-to-TSP (mg/m3) ratio is 5.3, whereas in our study the ratio was 4.4. Clearly, the SS smoke characteristics are similar in both studies. We are confident that any other researchers could duplicate our results were they so inclined. Finally, concerning reproducibility, we have now completed studies with cockerels exposed to the SS smoke generated by a steady state of one cigarette and have found significant increases in plaque sizes among the exposed cockerels. These results and associated “field” measurements
It would be helpful if the authors could provide a definition of paroxysmal atrial fibrillation (PAF). Do they refer to patients with evidence of paroxysms of atrial fibrillation interspersed with phases of sinus activity in the same Holter ECG tape, or by PAF do they imply that their patients were found intermittently to be in atrial fibrillation over relatively longer periods of time, as diagnosed by more than one Holter ECG tape? Clarification of this may be important for both research and clinical environments.

John E. Madias, MD
Department of Cardiology
Mount Sinai Services
Mount Sinai School of Medicine
Elmhurst, New York

References

Reply
We are grateful to Dr Madias for his interest in not only our recent work but also previous work. We have investigated a new technique to diagnose arrhythmia by integrating the coupling interval-dependent characteristics, i.e., successive RR interval plotting. Analyzing the massive data of RR intervals by our methods uncovers the hidden characteristics of various arrhythmias, which are not otherwise recognizable.

Our aim in the recent work was to introduce the RR interval plotting for diagnosing aberrant ventricular conduction and ventricular ectopy in atrial fibrillation.

The first concern of Dr Madias is that we stated the etiological, prognostic, and therapeutic importance on the differentiation between aberrant ventricular conduction and ventricular ectopy in atrial fibrillation without citing any relevant literature. He also pointed out that the small sample sizes of our study do not withstand such a thesis.

A starting point of our investigation began from the situation when we hesitated to treat the successive wide QRS complexes observed in atrial fibrillation in acute myocardial infarction. There is considerable evidence1-3 that the presence of ventricular ectopies predicts mortality after acute myocardial infarction. If we can easily diagnose the wide QRS complexes in atrial fibrillation as ventricular ectopies by noninvasive methods, we could identify the patients with atrial fibrillation and ventricular ectopies after acute myocardial infarction at high risk for sudden cardiac death. However, at that time we did not have any diagnostic tools to definitely differentiate ventricular ectopy from aberrant ventricular conduction in atrial fibrillation other than intracardiac ECG. Therefore, we thought that differentiation between aberrant ventricular conduction and ventricular ectopy in atrial fibrillation had etiological, prognostic, and therapeutic importance. It is beyond our intention, however, to conclude the prognostic and therapeutic importance in patients with atrial fibrillation in this report. The small sample sizes do not withstand to support such a thesis, as Dr Madias pointed out. Again, the focus of our study was not to investigate the etiological, prognostic, and therapeutic importance of the patients with atrial fibrillation and ventricular ectopies but to develop a noninvasive method to differentiate ventricular ectopy and aberrant ventricular conduction in atrial fibrillation. The prognostic and therapeutic investigation of the patients with atrial fibrillation and ventricular ectopies could be performed after establishing our method.

The second concern is a definition of paroxysmal atrial fibrillation. We referred to patients with evidence of paroxysmal atrial fibrillation interspersed with periods of sinus rhythm in the same Holter ECG tape.

Akiko Chishaki Suyama, MD
Research Institute of Angiography and Cardiovascular Clinic
Kyushu University School of Medicine
Fukuoka, Japan

Increased Aortic Impedance
The recent article by Eaton et al1 reports some very interesting and important findings in the comparative differences in changes in oscillatory and steady components of arterial hemodynamics in the early stages of cardiac failure in dogs. The results are significant in that they not only confirm the importance of the pulsatile arterial function on the heart but also show that these occur before changes in peripheral resistance, a result with major implications in understanding adaptive changes both in the heart and in the complex arterial load. The major change in the paced dogs (as described in the title of the article) is an increase in aortic impedance, a principal component of which is characteristic impedance. Pacing also produced a significant fall in mean arterial pressure. The authors rightly address the significance of passive effects on aortic impedance in relation to changes in arterial compliance. They state that a reduction in mean pressure should lead to a decrease in characteristic impedance due to passive effects of distending pressure. The opposite was found, so they state that vascular compliance may have actually decreased to a much greater degree than that determined by characteristic impedance, and major conclusions are drawn with respect to active effects of vascular tone or structural changes, with ensuing speculations involving the distribution of angiotensin II receptors throughout the arterial tree. However, the concomitant effect of reduction in aortic diameter due to the decrease in mean pressure was not considered. If this is taken into account, it can be shown that the increase in aortic characteristic impedance can be almost totally explained by this passive effect.

From the water hammer formula,2

\[
Z_c = \rho \cdot c / A = \rho \cdot c / \pi R^2
\]

where \(Z_c\) is characteristic impedance, \(\rho\) is blood density, \(c\) is wave velocity, \(A\) is lumen area, and \(R\) is radius.

From the Moens-Korteweg relation,7

\[
c = (\pi h / 2R)^{1/2}
\]

where \(E\) is Young’s modulus of the arterial wall and \(h\) is wall thickness.

It is unlikely that during the 48 hours of pacing, substantial structural changes would occur in the material of the aortic wall to cause changes in \(E\) or \(h\) as well as blood density, so from Equations 1 and 2,

\[
Z_c = K \cdot R^{-2.5}
\]

where \(K\) is a constant.

References
Aberrant ventricular conduction and ventricular ectopy.
J E Madias

Circulation. 1994;89:2944-2945
doi: 10.1161/01.CIR.89.6.2944

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circ.ahajournals.org/content/89/6/2944.citation