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The Effects of Aging on Atrial Endocardial Electrograms in Patients with Paroxysmal Atrial Fibrillation

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Summary

Background: The prevalence of atrial fibrillation (AF) has been reported to increase with advancing age. Histologic studies in AF have demonstrated that the percentage of fibrosis and degenerative changes in the atrial muscle increase significantly with age.

Hypothesis: This study was undertaken to assess the influence of advancing age on atrial endocardial electrograms recorded during sinus rhythm in patients with paroxysmal atrial fibrillation (PAF), which had not been assessed previously.

Methods: Right atrial endocardial catheter mapping during sinus rhythm was performed in 111 patients with PAF to evaluate the influence of advancing age on atrial endocardial electrograms. The bipolar electrograms were recorded at 12 sites in the right atrium, and an abnormal atrial electrogram was defined as lasting ≥ 100 ms, and/or showing eight or more fragmented deflections.

Results: In all, 1,332 right atrial endocardial electrograms were assessed and measured quantitatively. The number of abnormal atrial electrograms in patients with PAF showed a significantly positive correlation with age ($r = 0.34$; $p < 0.0005$). Patients aged > 60 years had a significantly greater mean number of abnormal electrograms (2.58 ± 2.05) than those aged < 60 years (1.43 ± 2.03; $p < 0.004$). The longest duration ($r = 0.35$; $p < 0.0005$) and the maximal number of fragmented deflections ($r = 0.29$; $p < 0.005$) of atrial electrograms among the 12 right atrial sites also showed a significantly positive correlation with age.

Conclusions: Aging alters the electrophysiologic properties of the atrial muscle in patients with PAF. Elderly patients have a significantly greater abnormality of atrial endocardial electrograms than do younger ones. There is a progressive increment in the extension of altered atrial muscle with advancing age in patients with PAF.

Key words: aging, paroxysmal atrial fibrillation, atrial muscle, atrial endocardial mapping

Introduction

It is well known that atrial fibrillation (AF) is not an electrophysiologically homogeneous process. Several predisposing factors may provide the background for this tachyarrhythmia to occur. Elderly subjects are particularly prone to develop AF, and changes of the atrial muscle with advancing age may be a factor accounting for this phenomenon. Davies and Pomerance reported that AF in some aged patients was associated with loss of muscle fibers in the sinoatrial node and its approaches without any clear pathological cause.[1] Muscle loss with advancing age was found to be accompanied by an increase in fibrous tissue in both the sinoatrial node and the internodal tracts.[2–4] It was strongly suggested that muscle loss and increase of fibrosis in the atria is a slow but continuous process starting at about 60 years of age.[3]

Since aging has a profound effect on structural changes of the atrial muscle, and since fractionated atrial endocardial electrograms may reflect nonsynchronized, delayed local electrical activity through a diseased atrial muscle,[5] it seems reasonable to assume that there may be detectable age-induced changes in atrial endocardial electrograms in patients with paroxysmal atrial fibrillation (PAF). To the best of our knowl-

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edge, this is the first study designed to clarify the influence of advancing age on atrial endocardial electrograms recorded during sinus rhythm by means of intra-atrial catheter mapping in patients with PAF.

Methods

Study Patients

A total of 111 nonconsecutive patients referred to the Nagasaki University Hospital for electrophysiologic evaluation of their arrhythmias underwent right atrial endocardial mapping in sinus rhythm during the course of the studies. Excluded from the study protocol were patients with organic heart disease or congestive heart failure, as well as those showing atrial enlargement on echocardiography.

The study comprised 111 patients (35 women, 76 men, age range 19–80 years, mean age 57.0 ± 14.1) with PAF. There were 55 patients with idiopathic PAF, 33 patients with sick sinus syndrome, and the remaining 23 had Wolff-Parkinson-White syndrome. The PAF in all patients was well documented by means of conventional electrocardiography (ECG), bedside ECG monitoring, or at least two ambulatory 24-h Holter recordings. The sinus node recovery time was measured in all patients after an atrial overdrive pacing[6, 7] at rates of 70 to 210/min, for a period of 1 min at each level.

Electrophysiologic Study

After giving informed consent, all patients were studied in the postabsorptive, nonsedated state. The present investigation complies with the declaration of Helsinki. Electrophysiologic evaluation was performed after approval of the study plan by the regional Ethics Committee. All drugs were discontinued at least 72 h before the procedure. No patient received amiodarone.

The intra-atrial catheter mapping technique was performed with bipolar catheter electrodes (No. 6F USCI, Div. C.R. Bard, Billerica, Mass., USA) that were inserted percutaneously into the femoral and subclavian veins and advanced into the right atrium under fluoroscopic guidance. The distance between the electrodes was 10 mm and the width of the electrode ring was 2 mm. All the right atrial endocardial electrograms were recorded during sinus rhythm at a fixed gain setting accompanied by a 0.2 mV = 3 mm calibration signal, and were filtered at 50 to 1,000 Hz. The baseline of recordings was stable for each patient. The atrial endocardial electrogram and three surface ECGs (I, aVF, V_1) were displayed on a multichannel oscilloscope (polygraph MIC-8800T, Fukuda-Denshi Inc., Tokyo, Japan) and simultaneously recorded at a paper speed of 100 mm/s on a 12-channel, ink-jet recorder (Siemens-Elema 804, Siemens-Elema, Solna, Sweden). All data were stored on magnetic tape throughout the entire electrophysiologic study. The atrial electrograms remained constant and reproducible at each recording site in individual patients.

The intra-atrial catheter mapping procedure has been described previously.[8, 9] In each patient, the bipolar electrograms were recorded from 12 sites in the right atrium, that is, atrial electrograms were recorded from the anterior, posterior, lateral, and medial aspects of the high, middle, and low right atrium. The high and middle atrial sites were mapped by the catheter inserted through the femoral vein, but the low atrial sites were mapped through the subclavian vein. No complications were noted in any patient as a result of these maneuvers. Stability was ensured by recording at each site for a minimum of 10 s and by using a loop configuration of the catheter. The position of the catheter tip was verified by multiple- or single-plane fluoroscopy in the presence of at least two experienced physicians familiar with the right atrial endocardial mapping procedure. Particular attention was paid to assure that all instruments were properly isolated and grounded.

Definitions

The duration of an atrial electrogram was defined as the time from the beginning of the earliest electrical activity deviating from the stable baseline value to the last point of the atrial electrogram at which the baseline value was crossed. The number of fragmented deflections was measured by counting the number of downward deflections.[8]

In a prior study[8] we defined quantitative standards for normal bipolar electrograms based on the measurements obtained from 516 atrial electrograms in 43 patients with normal sinus node function and without PAF. The mean duration and the mean number of fragmented deflections of these patients were 72 ± 11 and 3.9 ± 1.3 ms (mean ± standard deviation [SD]), respectively. Atrial electrogram values > 2 SD of these mean values were defined as normal. Hence, an abnormal atrial electrogram was defined as having a duration of ≥ 100 ms and/or eight or more fragmented deflections.

Data Analysis

Results are expressed as the mean values ± SD. Statistical significance was determined by using the Student's *t*-test for unmatched pairs. Prevalence was compared using the chi-square test. Correlation coefficients were determined by linear regression analysis. The duration and the number of fragmented deflections of the atrial electrograms were assessed at each site by at least two independent observers. A minimum of five to eight atrial complexes of uniform morphology were assessed at each of the 12 sites of the right atrium, and values with an interobserver variability of ± 5 ms were excluded from this investigation.

Results

In all, 1,332 atrial endocardial electrograms were assessed and measured quantitatively in the present study. The longest duration and the maximal number of fragmented deflections of atrial electrograms among the 12 right atrial sites were assessed in each patient. In addition, the number of abnormal atrial electrograms in each patient was also determined.

TABLE I Electrophysiologic data on atrial endocardial electrograms in patients <60 and ≥60 years of age

Age	Number of AAE per patient	Longest duration	Maximal number of deflections	Incidence of AAE
< 60 Years	1.43 ± 2.03 [a]	95.9 ± 14.8 ms [b]	8.04 ± 2.28 [c]	30/56 (54%) [d]
≥ 60 Years	2.58 ± 2.05	103.7 ± 14.6 ms	9.13 ± 2.72	46/55 (84%)

[a] $p < 0.004$; [b] $p < 0.01$; [c] $p < 0.03$; [d] $p < 0.001$.
Abbreviations: AAE = abnormal atrial electrograms, PAF = paroxysmal atrial fibrillation.

Of the 111 patients with PAF included in this investigation, there were 56 who were < 60 years of age. On the other hand, there were 55 patients whose age was ≥ 60 years. Abnormal atrial electrograms were observed in 46 (84%) of these 55 patients; $p < 0.001$ (Table I).

The mean number of abnormal atrial electrograms per patient as well as the longest duration and the maximal number of fragmented deflections of atrial electrograms were significantly greater in the patients aged > 60 years than those in younger patients with PAF.

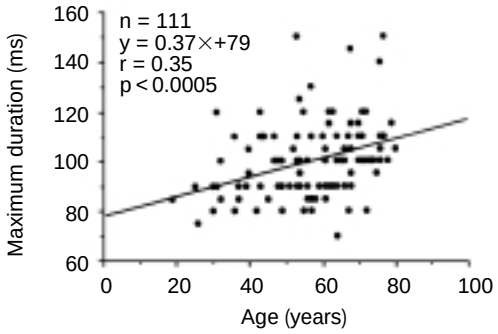

FIG. 1 Correlation between age and the longest duration of atrial electrograms among the 12 right atrial sites in each patient with paroxysmal atrial fibrillation. The linear regression line, equation, and correlation coefficient are shown.

The correlation between the longest duration of atrial electrograms and age is shown in Figure 1. There was a significant positive relationship ($r = 0.35$; $p < 0.0005$). The comparison of the maximal number of fragmented deflections of atrial electrograms with age revealed a significant positive correlation (Fig. 2). The correlation coefficient (r) was 0.29; $p < 0.005$.

The correlation of the total number of abnormal atrial electrograms in each patient with PAF and age is shown in Figure 3. There was a significant positive relationship ($r = 0.34$; $p < 0.0005$).

Discussion

Atrial fibrillation is one of the most common arrhythmias encountered in adult life, and it is known to be the most common underlying tachyarrhythmia in the diseased heart. There are many precipitating conditions that provide the setting in which AF develops, and aging may be a factor accounting for its occurrence. The process of aging and its effect on the histologic appearance of the conduction system of the heart have been described insufficiently. Some investigators have observed that normal histologic changes in the atrial muscle occur with advancing age. These include a reduction in the number of myocardial cells within the sinus node, a generalized loss of atrial myocardial fibers in the vicinity of the internodal tracts, as well as an increase in the quantity of connective tissue, which leads to an apparent loss of myocardial fiber continuity.[2–4] Davies and Pomerance reported that in some aged

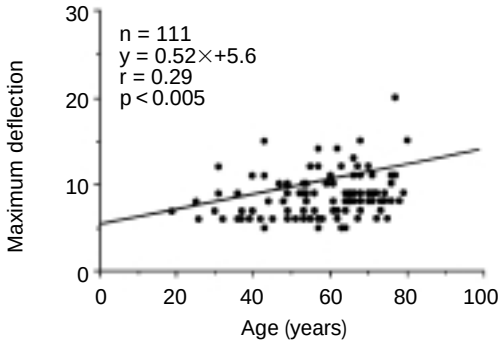

FIG. 2 Correlation between age and the maximal number of fragmented deflections of atrial electrograms among the 12 right atrial sites in each patient with paroxysmal atrial fibrillation. The linear regression line, equation, and correlation coefficient are shown.

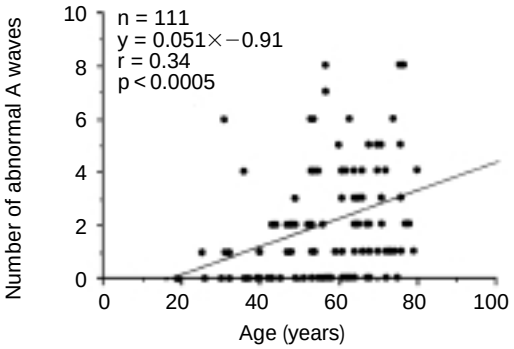

FIG. 3 Correlation between age and total number of abnormal atrial electrograms in each patient with paroxysmal atrial fibrillation. The linear regression line, equation, and correlation coefficient are shown.

patients AF was associated with loss of muscle fibers in the sinoatrial node and its approaches without any clear pathological cause.[1] Erickson and Lev have shown degenerative changes in the conduction system with age.[10]

With this histologic background in mind, changes in the electrophysiologic properties of the atrial muscle with advancing age can be expected. Indeed, dispersion and lengthening of atrial refractoriness with aging have been reported.[11–13] The demonstration of electrophysiologic changes in the atrial muscle with age[14–16] is consistent with the concept that electrophysiologic functional changes are related to histologic changes of the conduction system of the heart with advancing age. Michelucci *et al.* suggested that aging modifies atrial refractoriness in a nonuniform manner, inducing a progressing increment of dispersion of atrial refractoriness.[11] They reported that aging induces a lengthening of atrial refractoriness only at the high right atrium, but not at the mid and low right atrium. Spach and Dober[17] demonstrated a nonuniform anisotropic atrium with advancing age. However, the influence of age on atrial endocardial electrograms has not been described so far. Our results indicate that aging also influences the characteristics of atrial endocardial electrograms recorded during sinus rhythm in patients with PAF.

In the present study, we have found a significantly positive correlation between age and the number of abnormal atrial electrograms in patients with PAF. Patients aged > 60 years had a significantly greater mean number of abnormal electrograms than younger patients. In addition, the longest duration and the maximal number of fragmented deflections of atrial electrograms among the 12 right atrial sites also showed a significantly positive correlation with age. Our results show a progressive increment in the extension of the electrophysiologically altered atrial muscle with advancing age in patients with PAF. A prolonged and fractionated atrial electrogram may reflect desynchronized local electrical activity related to a delayed and nonuniform anisotropic conduction through a diseased atrial muscle. Therefore, abnormal electrograms indicate areas of altered anatomy and conduction that are suitable substrates for reentrant arrhythmias.[5] Since abnormal atrial electrograms increase with advancing age, these electrophysiologic changes may account for the ease with which AF can develop in elderly patients.

Limitations

Certain limitations are inherent to this electrophysiologic study. In the present study, atrial endocardial electrograms were recorded only from the right atrium, hence our findings cannot be extrapolated to those of the left atrium. The interelectrode distance of bipolar catheters, the filter frequency settings, the high gain recordings, and the motion at the electrode-tissue interface may affect the recording of fragmented electrograms by the endocardial mapping technique.

The results of our study suggest that (1) the number of abnormal atrial electrograms in patients with PAF has a significantly positive correlation with age, (2) patients with PAF aged ≥ 60 years have a significantly greater mean number of abnormal atrial electrograms than younger ones, and (3) the longest duration and the maximal number of fragmented deflections of atrial electrograms have a significantly positive correlation with age.

Conclusion

Aging alters the electrophysiologic properties of the atrial muscle in patients with PAF. Elderly patients have a significantly greater abnormality of atrial endocardial electrograms than younger ones. There is a progressive increment in the extension of altered atrial muscle with advancing age in patients with PAF.

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