

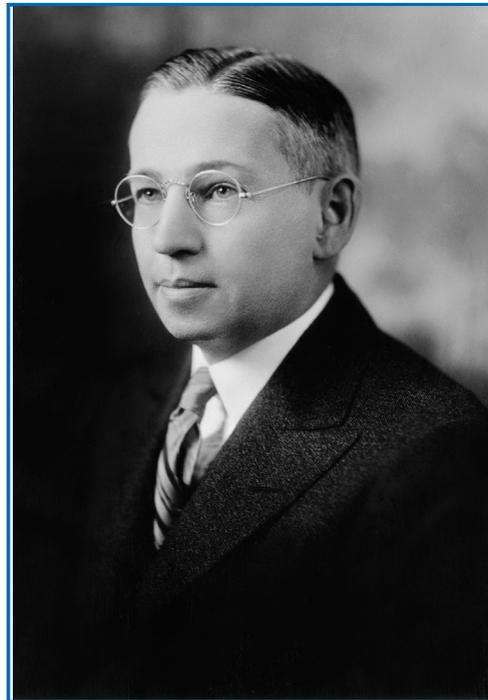
Survival With Auricular Fibrillation: The View From a Century Ago at the Mayo Clinic

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Atrial fibrillation is a common disease affecting millions of Americans. A century ago, it was a less regularly recognized phenomenon. With the advent of the electrocardiogram (ECG), this arrhythmia could be more readily identified. Frederick Willius, the first specialist in cardiology at the Mayo Clinic Rochester, became interested in the survival of patients with this condition. Using the tools at hand, he studied the outcome of 500 patients found to have ECG changes consistent with auricular fibrillation, as the condition was known at that time. Using mailed questionnaires, he examined the outcomes of death and death from cardiac causes and attempted to create a control group as well as a demographically matched subgroup analysis. Despite limitations, which he acknowledged, he demonstrated a worse outcome for these patients as well as the value of the ECG in diagnosing heart disease.

Frederick A. Willius was one of the first academic cardiologists in the United States. After graduation from medical school and internship at the University of Minnesota in 1915, he began a 3-year fellowship at the Mayo Clinic in Rochester, Minnesota. Dr Henry S. Plummer, who had established an electrocardiography laboratory the previous year, assigned Willius to work with Dr John M. Blackford on this relatively new technology, which had been first used in the United States in 1909 in New York City.¹ Willius published his first paper 8 years later, in 1917, on chronic heart block.² In 1923, Willius organized a section of Cardiology.³ He wrote a book about ECG interpretation in 1929 and promoted the use of the ECG for both clinical and research use.⁴

In 1919, Willius presented his research into Auricular Fibrillation and Life Expectancy, which was published that year in the collected papers of the Mayo Clinic as well as *Minnesota Medicine* in 1920. He noted



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that “the most important and most frequent disorder of the cardiac rhythm is that due to fibrillation of the auricles.” He also realized that auricular fibrillation (AF) could occur in a variety of heart diseases and, to understand the prognosis, it had to be examined as the “sum-total of evidence, subjective and objective...” He suggested that understanding the impact of this arrhythmia was important in establishing the patient’s prognosis, although he felt the most important factor, cardiac efficiency, was “as yet” unmeasurable. The object of this study was to “corroborate clinical impressions with statistics.”⁵

Willius identified 500 cases over 4.5 years with ECG evidence of AF. He then subdivided the cases by the presence of arborization (interventricular conduction delay), the presence of premature ventricular contractions

(PVCs), the combination of the 2, and mitral valve disease. He also examined the outcome of patients with aortic valve disease, chronic myocarditis, hypertensive disease with and without nephritis, and myocardial disease due to thyroid disorders. He identified 500 additional cases as a control group by gender and age who received ECGs without evidence of AF. Letters were sent to the patients with a brief question about their cardiac health and to relatives inquiring about the cause of death. In the case of nonresponse, follow-up letters were sent. He recognized the potential limitations but wrote: “The cases have been group for comparative study, and while the classification is not without certain objections, its employment is quite satisfactory.” The fact that some responses were missing, that some came from physicians, whereas others came from family, were minor defects, overbalanced by the “distinct value” of the large series.⁵

Willius received 367 replies from the 500 cases; 98 (36.9%) of the patients were identified as having cardiac demise, broken down by age. This compared with his control group, which demonstrated 38 (16.2%) cardiac deaths. Using modern statistical analysis of his data, the *P* value is <0.001. A twice-higher rate of cardiac mortality was seen in patients with PVCs; however, this difference was less pronounced with arborization, and no difference was seen with the combination of PVCs and arborization and AF than those without AF. Both mitral stenosis and insufficiency were associated with a higher rate of cardiac death.⁵

Discussion of the relevance of the study ensued. Dr S. Marx White of Minneapolis noted that the average practitioner, without access to ECG, might not recognize this condition and its significance and its value in the administration of digitalis. Dr S. P. Pres, also of Minneapolis, claimed that AF was incurable and a late complication of heart disease; further, he noted its importance in valvular

leakage. Dr Willius concluded by emphasizing the importance of the ECG as an adjunct to the careful clinical examination in making the diagnosis.⁵

The survival of patient with AF remains an important topic a century later.⁶ Despite limitations in data collection, Dr. Willius was able to amass a large series of cases. He attempted to construct a control group and performed subgroup analysis with age and gender matching and used descriptive statistics, all without the benefit of statistical modeling. Most importantly, he emphasized the clinical impact of auricular fibrillation, the value and superiority of the ECG as a diagnostic tool, as well as the impact of the subclassing of clinical diagnosis on the interpretation of clinical research.⁵

Abbreviations and Acronyms: AF = auricular fibrillation; ECG = electrocardiography; PVC = premature ventricular contractions

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