HISTORY OF ELECTROCARDIOLOGY

Introductory Note to a Translated Classic Article of L. S. Fridericia: L. S. Fridericia. Die Systolendauer im Elektrokardiogramm bei normalen Menschen und bei Herzkranken (*The Duration of Systole in an Electrocardiogram in Normal Humans and in Patients with Heart Disease*). Part I: Beziehung zwischen der Pulsfrequenz und der Dauer des Ventrikelelektrokardiogramms bei normalen Menschen in der Ruhe (*Relationship of the pulse frequency and the duration of the ventricular electrocardiogram in normal humans at rest*). Acta Med Scand 1920;53:469–486

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The invention of the electrocardiogram was reported by Einthoven in 1903, and electrocardiography was still in its infancy when the relationship between the duration of electrical systole (now referred to as the QT interval) and the pulse frequency (heart rate) was reported independently in 1920 by Bazett¹ and Fridericia.² Bazett identified a direct relationship between the QT interval and the square root of the pulse period (RR interval), and his article was published in English in *Heart*. Fridericia found that the duration of the QT interval was related to the cube root of the RR interval, and his article was published in German in *Acta Medica Scandinavica*. These independent publications on ventricular repolarization by Bazett and Fridericia in the same year have stood the test of time and have been referenced extensively throughout the past 80 years. To my knowledge, the original article by Fridericia has not been previously translated into English, so I thought a translation would

be worthwhile for those who don't read German. In this regard, I am indebted to Gisela Beutner, Ph.D., a Research Assistant Professor in the Department of Pharmacology & Physiology at the University of Rochester School of Medicine and Dentistry, who translated Fridericia's original article from German to English.

Who was Dr. L. S. Fridericia? He was a Danish physician who was professor of medicine and physiology in Copenhagen in the first part of the 20th century. His publication on the duration of electrical systole in 1920 may have been one of his only contributions to electrophysiology. He was also involved in pH and acid-base determinations in various tissues including the red blood cell,³ and he investigated the relationship between night blindness and nutrition.⁴ What is clear from these publications is that Dr. Fridericia was a skilled physician and scientist involved in the study of physiologic phenomena.

Fridericia recognized the need for standardized measurements of the normal duration of human ventricular repolarization, an electrical systolic interval newly available from the recently introduced electrocardiogram. Prior hemodynamic studies showed that the duration of mechanical ventricular contraction was shortened at faster heart rates. Fridericia reasoned that similar changes would probably be found when electrical systole was measured at different heart rates. The question of course was: What was the relationship? He studied just 50 subjects, but he made sure they were healthy normal individuals and were representative of a wide age range from young children to octogenarian adults with involvement of both males and females. Even at that early stage in electrocardiography, the recording speed of the photographic plates was 25 mm/sec with 1 mm time duration equal to 0.04 seconds. Fridericia was concerned about the accuracy and the error rate in the measurement of both the pulse period (RR interval) and the duration of the ventricular electrocardiogram (QT interval). He appreciated the fact that there were potentially larger errors in measurement of the QT interval than of the RR cycle length, and he carefully evaluated the variation in the measurement of these intervals.

Figure 1 in the original manuscript graphically displays the relationship between the QT interval and the RR cycle length or heart rate. The relationship was evaluated through mathematical modeling. To find a simple relationship between QT and RR, Fridericia limited the equations he used so that no more than two constants were used in the analysis. Over the range of RR intervals observed, an exponential equation with two constants optimized the fit of the data with a minimal average error. He found that QT could be predicted accurately from the following formula: $QT = K (RR^{0.3558})$. Fridericia felt that 0.3558 was interchangeable with 0.3333, and thus the cube-root relationship. His final equation was:

$$QT = 8.22^3 \sqrt{RR}, \quad \text{where QT and RR are values in 100th of a second.}$$

The main table in Fridericia's article provides the difference in the measured and calculated QT values in all 50 subjects. He found an average error of 0.015 seconds and concluded that only QT variations more than three times the average error (0.045 sec) should be considered outside the normal range. At a heart rate of 60 bpm (RR = 100 when expressed as 100th of a second), the calculated average QT interval by the above formula is 0.382 seconds. Using this approach, the upper normal value for the QT interval at a heart rate of 60 bpm is 0.427 seconds (0.382 sec + 0.045 sec), and QT values >0.43 seconds are considered prolonged. It is amazing that this value for an abnormally prolonged QT interval at a heart rate of 60bpm is essentially what we still use today. The concept of the corrected QT interval (QTc), based on the same empirical formula, would be introduced a little later.

A lot has transpired since Fridericia's publication in 1920. Recent investigations indicate that when a range of heart rates is explored in normal individuals, the value of the exponent in Fridericia's QT formula may be different in different individuals, i.e., each individual may have his or her own exponent value in the Fridericia formula, a reflection of our genetic individuality. We are fortunate to have had giants like Einthoven, Bazett, and Fridericia in electrophysiology, for they provided us with a sound foundation for investigations into the heart rate dynamics of ventricular repolarization that are currently taking place in the 21st century.

REFERENCES

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