Investigative Electrocardiography in Epidemiological Studies and Clinical Trials
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Preface

This book on investigative electrocardiography is addressed to investigators who are using electrocardiology as a research tool in epidemiological or clinical research or in investigations on possible adverse responses of new pharmacological agents. The primary emphasis of the book is on prognostic implications of ECG abnormalities in the conditions covered, including the prevalence and incidence of ECG abnormalities in contrasting populations.

We excluded from our book cardiac disorders with a relatively low population prevalence that otherwise may be of great clinical interest. We also decided to exclude acute myocardial infarction because we had only limited resources available on this topic from our population studies and from those clinical trials in which we have personally participated in the classification of trial endpoints within the framework of an ECG research center.

Clinical trials are a relatively new area of electrocardiology. However, electrocardiography has become a most valuable research tool in clinical trials and in investigations on morbidity and mortality risk associated with various clinical and subclinical conditions. It has also become a crucial research tool in investigating adverse cardiac events associated with administration of new drugs. Evaluation of QT prolongation plays a central role in these investigations. As a possible marker of malignant arrhythmias, it is used by regulating agencies in their decision process for approval of new pharmacological agents.

Part 1 of this book begins with an account of ventricular excitation and repolarization (Chapter 1), followed by Chapter 2 composed to facilitate the understanding of ECG leads. Chapter 3 is a review of ionic channel functions in relation to ECG waveforms and their role in drug effects. Heart rate and heart rate variability evaluation is covered next (Chapter 4). Arrhythmic conditions selected include epidemiological aspects of atrial flutter and fibrillation and other atrial dysrhythmias (Chapter 5) and the role of ectopic ventricular complexes (Chapter 6). Chapter 7 provides insights and a critical evaluation of electrocardiographic left ventricular hypertrophy, and Chapter 8 covers ventricular conduction defects. The last three chapters cover epidemiological aspects of old myocardial infarction (Chapter 9), the importance of primary repolarization abnormalities (Chapter 10), and finally, a critical evaluation of QT prolongation and QT dispersion (Chapter 11). An important component in this last chapter is the establishment of appropriate adjustment functions for QT interval, to overcome critical problems associated with the traditional Bazett’s formula and other power functions currently used for QT rate adjustment.
Each chapter starts with a synopsis summarizing the importance of the topic. The main text in each chapter covers the mechanism, classification problems, prevalence and incidence, and predictive value of the abnormality.

Part 2 of the book contains an extensive series of tables listing normal standards by gender, age (40–79 years), and ethnicity (Caucasian white and African–American), established from large groups of healthy North-American populations. No previous properly established normal standards are available for African–American men and women or for older white women, and only limited standards are available for vectorial parameters of ECG waves for any of these subgroups. These normal standards are presented as five sections: Section A, ECG intervals; Section B, ECG wave amplitudes; Section C, ECG vector components and spatial magnitudes at normalized time scale; Section D, ECG amplitudes at 10-ms intervals; and Section E, repolarization waveform vectors.

Many individuals have significantly contributed to the effort that was required for the completion of this book. The authors have closely collaborated for over a quarter of a century in operating a central ECG laboratory that has been in charge of computer analysis of major national health surveys conducted by the US National Center for Health Statistics and a series of large cardiovascular observational studies and clinical trials sponsored by the US National Heart, Lung, and Blood Institute. The authors wish to express their gratitude to the sponsors and participants of these studies, principal investigators, and their supporting staff. Our participation in several large clinical trials sponsored by the pharmaceutical industry has also been a valuable experience that has benefited the composition of this book.

The authors wish to acknowledge the collaborative efforts of the personnel of the central ECG laboratory that has operated in different locations under the name EPICARE. In particular, Dr. Ron Prineas, Dr. Zhu-Ming Zhang, and Charles Campbell, Wake Forest University, NC, and James Warren, Dalhousie University, have provided important support for this undertaking. The collaboration and friendship of Dr. Henry Blackburn since the earliest years of cardiovascular epidemiology has provided an important intellectual stimulus throughout these years.

Pentti Rautaharju and Farida Rautaharju
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