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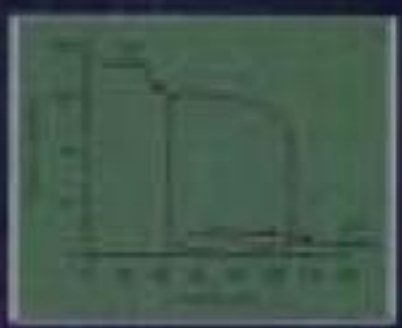
DIASTOLOGY

CLINICAL APPROACH TO DIASTOLIC HEART FAILURE



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Foreword

Doctors Klein and Garcia have attacked a controversial yet extraordinarily problematic clinical challenge with aggressiveness, insight, and thoroughness. Their text, *Diastology: Clinical Approach to Diastolic Heart Failure*, is one of the few organized efforts to bring together noted experts and synthesize today's knowledge base regarding this fascinating problem. The depth and breadth of topics covered in this text are extraordinary, and the editors and individual contributors are to be congratulated. The importance of this subject cannot be overemphasized because it is now well established that almost half of all patients admitted to the hospital for symptomatic congestive heart failure have relatively preserved or normal left ventricular systolic function. It is assumed that some degree of abnormality in diastolic function contributes to the presentation of these patients and, indeed, predicts decompensation. Knowing that well over 5 million patients in North America alone have heart failure makes, then, the importance of this syndrome high. The debate about syndrome nomenclature has been entertaining. Should we be referring to the difficulty as "diastolic heart failure" or "heart failure in the setting of preserved left ventricular systolic function"? Doctors Klein and Garcia are not shy about their opinion of facts, as the title of the text indicates.

Diastolic dysfunction can be defined as the inability of the heart to perform adequately under a normal filling pressure, and this generally results in impaired exercise tolerance resulting from varying combinations of inadequate forward cardiac output and elevated left ventricular end-diastolic pressure. Perhaps the most important intrinsic left ventricular abnormality is slowing of the rate of left ventricular relaxation and increased stiffness of the chamber. The nuances of this finding and, indeed, the spectrum of definitions are well characterized and addressed in this text.

Recognition of the importance of diastolic heart failure has been relatively recent, but there is now a large spectrum of data that gives us more precise information regarding the pathophysiology, epidemiology, and prognosis, and there are even a few recent trials studying therapy in these patients. Perhaps the latter is the most disappointing with little to guide us regarding the best approaches for reducing the substantive morbidity and mortality seen with this syndrome. Again, Doctors Klein and Garcia and their contributing authors are to be applauded for their thorough review of the current knowledge base regarding diastolic dysfunction and heart failure in the setting of preserved or relatively normal left ventricular systolic function. This text will capture the interests of clinicians, clinical investigators, and basic scientists interested in gaining insight into heart failure more generally.

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Foreword

In the past two decades, there have been remarkable advances in our appreciation of how cardiac diastolic function is important for patient well being. My first encounter with this occurred as a fellow in training in the early 1980s, when in Baltimore we were seeing so many elderly, predominantly females, with hypertension and hypercontractile left ventricles—but the seemingly paradoxical presentation with heart failure. It is interesting to reflect back on how ignorant we were back then with respect to the primacy of cardiac filling and relaxation and how far we have come since that time.

In this book, the field of diastolic function and dysfunction is fully dissected. All of the major intersecting processes, such as hypertension, coronary artery disease, pericardial disease, valvular abnormalities, diabetes, and so many others, are tackled. The recent surge in the use of biventricular "resynchronization" and atrio-ventricular optimization has markedly accentuated the role of the interaction of systole and diastole in clinical practice—and we still have much to learn in selecting patients who will benefit from this "big ticket" technology. The simple notion that ideal patients would have a markedly dilated heart with left bundle branch block certainly has not held up for long. Our enhanced understanding of ventricular interaction and diastole, per se, should make a difference. New and improved imaging modalities such as tissue Doppler imaging and strain rate imaging have given us a keener ability to quantify and differentiate "normal" and abnormal diastolic function. A variety of new indices, methods, and innovative imaging tools including torsion imaging will undoubtedly help illuminate the field in the years ahead.

The book is as good as it gets in laying out a comprehensive assessment of where we are and where we are going in the comprehensive field of diastology. Drs. Klein and Garcia and the superb group of authors they have engaged have done quite an exceptional job in providing a panoramic view of a very dynamic field. Cardiologists in training, those in practice who have an interest in cardiac physiology, and virtually all academic cardiologists and sonographers who want to enhance their understanding of the implications of cardiac relaxation and filling will benefit from this fine contribution to cardiovascular medicine.

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Preface

A 65-year-old woman with hypertension presents to the emergency room with shortness of breath. Chest x-ray shows interstitial edema, and two-dimensional and Doppler echocardiography demonstrate an ejection fraction of 60%, concentric left ventricular (LV) hypertrophy, atrial enlargement, and stage 2 (moderate) LV diastolic dysfunction. The brain natriuretic peptide level is elevated at 800 pg/dl. This prototypic patient has evidence of classical diastolic heart failure, which is the inability to fill the left ventricle with normal filling pressures. This timely book addresses how diastolic heart failure is diagnosed and treated. It also comprehensively discusses the general principles of diastolic dysfunction, including the molecular biology, hemodynamics, epidemiology, clinical presentation, and principles of treatment. The contents of this book are targeted to a broad audience encompassing noninvasive and invasive cardiologists, physiology scientists, cardiology fellows, and cardiac sonographers.

Multiple cardiovascular disorders cause diastolic dysfunction and subsequent diastolic heart failure. There is a raging controversy about whether diastolic heart failure exists as an independent entity or whether it is always accompanied by systolic dysfunction in the setting of a normal ejection fraction. In this book, we have elected to use the term *diastolic heart failure*; however, we recognize that systolic-ventricular interaction and arterial stiffening can definitely play a significant role in causing symptoms of heart failure in these patients. Why study diastolic heart failure? The answer is that a complete understanding of the pathophysiology of LV filling is essential to managing the patient with congestive heart failure syndromes. There has been a tremendous interest in diastology during the past 50 years, with over 16,000 original manuscripts published during this period.

Historical Perspective

Since the heart was determined to be a pump, most biologists and physicians have focused on the study of systolic function. However, as early as in the renaissance period, Leonardo da Vinci described that the lower cardiac chambers of the heart filled with blood by drawing it from the upper chambers. In the 1940s, Carl J. Wiggers proposed the term *inherent elasticity* to describe the passive properties of the heart. In the 1970s, cardiac physiologists assessed the properties of active ventricular relaxation and passive filling using invasive quantification of intracavity pressure and volume. During the following decade, clinicians recognized that diastolic heart failure was an important cause of congestive heart failure, and Doppler echocardiography emerged as an important noninvasive method to assess the diastolic filling properties of the heart. The term "diastology" was coined in the early 1990s; imaging modalities, such as Doppler tissue imaging, color M-mode Doppler, and magnetic resonance imaging (MRI), advanced our understanding of diastolic function. Over the past 10 years, new techniques and indices for assessing diastolic function have continued to evolve. Recent epidemiology-based studies have shown that diastolic heart failure is increasing in prevalence and that it is as common as systolic heart failure and just as fatal. In the past 5 years, there has been a shift from research in developing diagnostic techniques to large-scale clinical trials to determine targeted treatment for patients with diastolic heart failure.

Our Interest in the Field

In the late 1980s, Allan Klein started his interest in this field as a Canadian Heart Foundation fellow at the Mayo Clinic studying Doppler assessment of LV filling during acute myocardial infarction and after reperfusion. His first impression was that the quick bedside echocardiographic evaluation, including the mitral E/A ratio and deceleration time, was a simple but powerful measure of LV diastolic filling, relaxation, and prognosis. Also, he was struck by how the stages of diastolic filling related to the clinical exam, including the extra heart sounds (S3 and S4). As a student of the field, he also learned that the study of diastolic function was more complex than the simple analysis of the mitral E/A ratio. During his training, Dr. Klein was very fortunate to have excellent mentors, including Liv Hatle, Jamil Tajik, and James Seward. Dr. Mario Garcia developed his interest in the field while at the Cleveland Clinic in the early days of tissue Doppler echocardiography, color M-mode Doppler, and strain rate imaging. His clinical observations and hemodynamic validation of early annular velocities (E_m) and the slope of the flow propagation (Vp) as well as the relationship of mitral early filling/annular e wave (E/E_m) and mitral early filling/flow propagation slope (E/vp) as measures of LV filling pressure were important for the advancement of the field. Their interest led to many diastology symposiums where leaders congregated in Cleveland, Ohio, and Scottsdale, Arizona, to discuss their advances. These summits sparked our interest to publish a state-of-the-art book on diastology.

Contents of the Book

This book is organized into five main sections: basic determinants, diagnosis, specific cardiac diseases, emerging topics, and treatment. It includes a comprehensive analysis of the major areas of knowledge in this field from the molecular, genetic, and cellular mechanisms to clinical presentation and treatment of diastolic heart failure. This book discusses conventional and newer methods of diagnosis, including two-dimensional and Doppler echocardiographic techniques as well as cardiac MRI. An important practical chapter of how to actually perform a diastolic function examination written by one of the leading cardiac sonographers in the field

is also included. A review of the prototypical diseases that manifest diastolic dysfunction, including hypertension, coronary artery disease, hypertrophic cardiomyopathy, restrictive cardiomyopathy, and pericardial diseases, provides an important clinical perspective. Newer topics that are addressed include the role of neurohormones, pacing, aging, and vascular cardiac interactions in diastolic heart failure. Finally, the general treatment, echocardiographic guided therapy, and ongoing clinical trials are covered in depth by the leading experts in the field.

In the past, treatment of heart failure has focused purely on the treatment of systolic heart failure. However, there have been an increasing number of clinical trials, including The Candesartan in Heart Failure, Assessment of Reduction in Mortality and Morbidity (CHARM) preserved trial, the Perindopril for Elderly Patients with Chronic Heart Failure (PEP-CHF) trial, as well as ongoing studies, including the Irbesartan in Heart Failure with Preserved Ejection Fraction (I-PRESERVE) and the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trials, that address the treatment of diastolic heart failure. The importance of new drugs including endothelial receptor antagonists and glucose cross-link breakers that evaluate the targeted treatment of diastolic heart failure is also reviewed in this book.

Finally, it is important to recognize that the field of diastology is a fast-moving target and we have tried to be as current as possible while also avoiding overlap in the chapters.

We surely hope that you enjoy this exciting book.

Allan L. Klein
Mario J. Garcia

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