MYOCARDIAL METABOLISM IN HEALTH AND DISEASE ROBERT GROPLER, LINDA R. PETERSON VASKEN DILSIZIAN pdf

1: - NLM Catalog Result

The advent of myocardial metabolic imaging more than 30 years ago ushered in a paradigm shift in the clinical management of patients with ischemic and nonischemic heart disease.

Each new edition has been associated with significant expansion, revision, and updating, as well as significant changes in orientation that reflect new advances in the field. At the time of this fourth edition, nuclear cardiology is firmly established as a key noninvasive modality for the clinical evaluation of patients with cardiovascular disease. Concomitantly, there have been further advances in instrumentation, radiopharmaceutical development, and new clinical research, leading to additional understanding of clinical utility, cost-effectiveness, appropriateness, and relationship of imaging findings to patient outcomes. Nuclear cardiology has been incorporated into major large multicenter clinical trials. In addition, as other modes of cardiovascular imaging have approached maturity, there has been movement toward integrating the various imaging modalities under the broad umbrella of cardiovascular multimodality imaging. The cardiovascular imager of the future will likely be trained in more than one modality and will be housed in dedicated imaging centers that offer a variety of imaging approaches. In recognition of this trend, new chapters are included in this edition that provide additional focus on non-nuclear cardiovascular imaging modalities such as computed tomography, magnetic resonance imaging, and contrast echocardiography. The fourth edition continues to focus on nuclear cardiology and represents a major effort to incorporate new advances in clinical nuclear cardiology, thereby providing a road map for up-to-date clinical use. In addition, we seek to point out the new directions in which nuclear cardiology as well as integrated cardiovascular imaging are headed. Our goals in the fourth edition continue to be twofold: To meet these combined goals, the book has once again expandedâ€”now to a total of 45 chaptersâ€” and also includes a totally new and expanded atlas of case presentations to provide concrete examples of the clinical relevance of nuclear cardiology. Once again, the book is grouped into nine specific sections. Twenty of the 45 chapters, as well as the atlas, are totally new. An almost equal number of chapters have been eliminated, and, all remaining chapters have been revised, updated, and, in certain instances, consolidated. Section 1 addresses issues related to radiopharmaceuticals and tracer kinetics. The three chapters in this section provide information concerning tracer kinetics and cellular mechanisms of uptake, principles of myocardial metabolism as they relate to imaging, and the role of intact biological models in evaluating radiotracers. Section 2 deals with instrumentation. Section 3, as in the previous edition, contains two chapters dealing with cardiac function and performance, as evaluated by blood-pool imaging and gated SPECT imaging. Section 4 addresses major issues that relate to perfusion imaging and detection of coronary disease. The 12 chapters in this section address the issues of coronary artery disease detection by exercise and pharmacologic stress, their prognostic implications, assessment of myocardial perfusion imaging by magnetic resonance imaging, echocardiography, and positron emission tomography PET , and hybrid imaging. Specific chapters deal with computed tomography angiography and use of computed tomography to assess coronary artery calcification. Chapters also address cost-effectiveness as well as the appropriate use criteria for nuclear cardiology. A chapter also compares the various noninvasive approaches for assessment of myocardial perfusion. Section 5 focuses on disease- and gender-specific issues. Specific chapters focus on imaging in women, imaging for preoperative risk assessment, revascularized patients, patients with diabetes mellitus, imaging in xvii xviii Preface the heart failure population, imaging of patients receiving cardiotoxic chemotherapy, mental stress imaging, and the use of PET measurements of myocardial blood flow to evaluate cardiovascular pathophysiology and therapeutic efficacy. Section 6 addresses acute coronary syndromes. The two chapters in this section deal with imaging in the emergency department and risk stratification of patients with acute myocardial infarction, based on new data from a multicenter randomized trial. Section 7 contains four chapters focusing on myocardial viability. Viability assessment with SPECT studies, PET, and other techniques is addressed in three specific chapters, while an

additional chapter focuses on the pathophysiologic basis of hibernating myocardium. Section 8 contains three chapters on tracer-specific imaging techniques. Section 9 deals with new molecular approaches and contains three chapters dealing with molecular imaging of angiogenesis matrix metalloproteases and cell death, vascular abnormalities, and imaging of gene expression and cell therapy. Such techniques are primarily being evaluated in preclinical experimental models but have already shown promise in early clinical studies. The Atlas of Cases is the final section of the book and is designed to provide complementary information to the numerous clinical issues discussed in the text. It exemplifies the substantial clinical utility of nuclear cardiology and shows a variety of images set in their clinical context. This atlas is significantly expanded from the one included in the third edition. Zaret and George A. This underlying framework provides an essential basis for understanding and clinical interpretation of tracers, including the sensitivity of different tracers to indicate reduction of coronary flow reserve, the use and limitations of redistribution and reinjection, and the applications of tracers for indication of myocardial viability and prediction of recovery of myocardial contractile function. An example would be the curve that relates tracer uptake as a function of myocardial blood flow. There are certain basic relationships that govern the extraction, washout, and recirculation of tracers. These basic generic relationships facilitate the understanding of many different tracers used in various ways. As an introduction to perfusion tracers, the first part of this chapter will review the basic properties and cellular uptake mechanisms of a few of the single-photon emission computed tomography SPECT myocardial perfusion agents. We will employ a common solute absorption model to help understand the relationship of tracer extraction to capillary perfusion and use a simplified compartmental exchange model to help understand tracer redistribution. Comparing model predictions to experimental data will add some fascinating light to the mechanism of myocardial vasoregulation. Following this introduction, and in the light of our improved understanding of tracer kinetics, we will discuss specific clinical applications of the tracers commonly used for myocardial imaging. Thallium Thallium Tl is a radioactive potassium analog. This phenomenon is true of all diffusible flow tracers and will be discussed in detail in the next section of this chapter. Once inside the myocyte, Tl is not bound intracellularly and can diffuse back out into the circulation. As will be discussed in detail later, these uptake and redistribution kinetic properties form the basis of clinical assessment of myocardial perfusion and viability using Tl. The low-energy to 80keV x-ray photopeak can result in attenuation artifacts and the relatively long hour half-life limits the maximal dose that can be safely administered. Monovalent Cationic Technetiumm-Labeled Tracers Technetiumm 99mTc is a generator-produced isotope that is readily available and has a number of advantages over Tl for gamma camera imaging. The higher-energy keV principle photopeak is ideal for detection using standard collimated gamma cameras with less attenuation, and its short 6-hour half-life allows for a higher administered dose yielding improved count statistics. Over the years, there have been a number of 99mTclabeled myocardial perfusion imaging agents that have been investigated as replacements for Tl. The most successful ones to date are the lipophilic monovalent cationic agents, 99mTc-sestamibi sestamibi, Cardiolite and 99mTc-tetrofosmin tetrofosmin, Myoview , that are now widely used for clinical studies. Although these agents are members of two distinct chemical classes of compounds, isonitriles and diphosphines, respectively, they share several common properties. Unlike Tl, which utilizes a specific membraneactive transporter, these tracers are passively drawn across the sarcolemmal and mitochondrial membranes along a large electronegative transmembrane potential gradient, owing to their lipophilicity and positive charge. Although ATP is not directly required for the intracellular sequestration of cationic tracers, as it is for Tl, the influx and retention of these tracers are energy dependent because the presence of a normal electronegative transmembrane gradient is required. With irreversible injury, the mitochondrial and sarcolemmal membranes are depolarized, and the uptake of these cationic tracers is impaired. In addition to the lower plateau in extraction mentioned, another disadvantage to both sestamibi and tetrofosmin is the problem of photon scatter from the adjacent liver that can interfere with the interpretation of myocardial perfusion defects, particularly in the inferior left ventricular wall. Accordingly, there has been renewed interest in recent years to design improved cationic 99mTc-labeled

tracers that exhibit more rapid liver clearance. However, studies in both rats and dogs demonstrated that DBODC5 cleared more rapidly from the liver than either of these other cationic tracers, with virtually no liver activity observed after only 1 hour. At the present time, the first-pass extraction fraction studies have not been conducted using MPO. Thus, although the myocardial extraction fraction that is observed immediately after injection is very high, the rapid clearance of this tracer results in a loss of defect contrast within the first 5 minutes post injection. Thus, teboroxime is considered to be a pure perfusion tracer. Although teboroxime was approved for clinical imaging at the same time as sestamibi, its rapid dynamic myocardial clearance kinetics proved difficult to image 1 Overview of Tracer Kinetics and Cellular Mechanisms of Uptake using the relatively slow, single-head gamma cameras that were standard in the early s. With the exciting new generation of fast cardiac SPECT instrumentation that has recently become available on the market, there may be renewed interest in this tracer in the future. Like teboroxime, NOET exhibits a first-pass extraction fraction that is higher than either sestamibi or tetrofosmin, with flow-dependent differential clearance of the tracer from the myocardium. NOET is also believed to remain within the intravascular space in association with the endothelial layer. Experimental studies demonstrated that the myocardial clearance rate of NOET could be accelerated not only by increasing the flow rate but also by elevating the blood lipid concentration. In summary, the advent of the 99mTc-labeled myocardial perfusion imaging agents, particularly the lipophilic cationic tracers, sestamibi and tetrofosmin, represented a major advance by virtue of their superior imaging properties compared with Tl. Some aspects of these tracers may not be ideal, but in general they have shown excellent diagnostic accuracy and have fueled the growth of the field of nuclear cardiology for nearly 20 years. New SPECT perfusion tracers that exhibit both improved myocardial first-pass extraction fraction and more favorable biodistribution properties are clearly warranted. The outward and backdiffusion coefficients can be different. The extraction coefficient reflects the net loss in tracer concentration between the arterial and venous ends of the capillary. The relationship between blood flow and tracer extraction predicted by this model is shown graphically in Figure The term first-pass extraction is often used to characterize radionuclide tracers, but it is not often carefully defined. Since the extracted fraction of tracer is flow dependent, the first-pass extraction indicates the fraction of extracted tracer measured at baseline resting blood flow. The amount of tracer taken up by the myocardium shortly after bolus injection is the product of extraction fraction and myocardial blood flow per unit volume, denoted by the letter b. The curve with the functional form shown has been ubiquitous in representing myocardial uptake as a function of myocardial blood flow. If all the tracer atoms were extracted in a single pass through the capillary bed, the number of tracer atoms per unit volume of tissue would then be proportional to the fraction of cardiac output perfusing the unit volume of tissue. The only tracers that approximate this ideal are microspheres. The tracers used for clinical imaging of myocardial blood flow are not completely extracted. For these tracers, the fraction of tracer extracted on passing through a capillary bed depends on the blood flow through the capillary bed. A model based on the work of Gosselin and Stibitz 22 provides insight into this process. The model is that of a diffusible tracer traveling through a cylindrical capillary. The tracer can diffuse outward from the blood across the capillary endothelium, but it can also diffuse back into the blood from outside 1.

2: NEW DISCOVERIES FOR PREVENTION AND TREATMENT OF HEART DISEASE - PDF

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4: Cardiac CT, PET and MR

Cardiac health is dependent on the heart's ability to utilize different substrates to support overall oxidative metabolism to generate ATP. Indeed, a loss in plasticity in substrate preference is characteristic of a variety cardiac diseases such as diabetic heart disease, in which fatty acid metabolism predominates, and dilated cardiomyopathy, in which glucose metabolism predominates.

5: Cardiac CT, PET and MR : Vasken Dilsizian :

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4 PET Assessment of Myocardial Perfusion, 95 5 Myocardial Metabolism in Health and Disease, Robert J. Gropler, Linda R. Peterson & Vasken Dilsizian.

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