The Evolution of Cardiac Nuclear Imaging

Frank M. Bengel[1] and Marcelo F. Di Carli[2]

[1]Department of Nuclear Medicine, Hannover Medical School, Hannover, Germany; and [2]Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts

Although cardiovascular disease remains the leading cause of death worldwide, there has been tremendous success in its treatment over the last few decades, leading to a dramatic decline in age-adjusted cardiovascular mortality (*1*). This success is strongly attributed to effective management of acute, deadly manifestations such as myocardial infarction (*2*). Although more patients survive, they enter a subsequent stage of chronic disease with an injured heart. The prevalence of chronic heart failure is rising accordingly, posing a major challenge to the cardiovascular care of the future (*3*).

This evolution of cardiovascular disease epidemiology is paralleled by an evolution of cardiovascular therapy. The currently available powerful armamentarium of interventional and surgical procedures, implantable devices, and antithrombotic and heart disease risk factor–modifying drugs is continuously expanded by the development and introduction of novel treatments with an ever-increasing specificity that seeks to modify selective molecular pathways or even entire systems of molecular and cellular interaction (*2*,*4*,*5*). The goal of such novel therapies is to enhance myocardial repair or even provide a causative modification of cardiac disease, so that—beyond the effective treatment of acute events—the development of a chronic disease state can be prevented or reversed. Similar to other fields of molecular medicine, such targeted therapies, based on, for example, antibodies, nanoparticles, RNAs, or engineered cells, will be expensive, and because of their specific nature, they are not expected to work in everybody. This emphasizes the need for effective biomarkers to implement a personalized approach toward therapy guidance. Accordingly, the quest for biomarkers in personalized medicine presents an opportunity for noninvasive imaging (*4*,*6*).

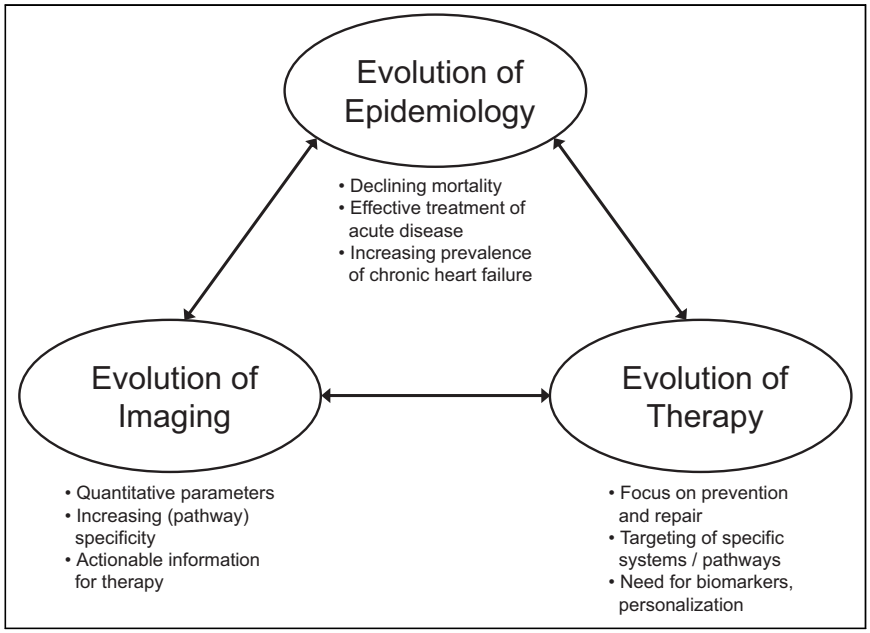

FIGURE 1. Evolution of cardiovascular medicine: interplay between cardiovascular disease epidemiology, therapy, and imaging-based diagnostic tools.

The increasing range and increasing specificity of therapeutic options in cardiology are paralleled by an increasing range and increasing specificity of diagnostic imaging options, adding another layer to the evolution of cardiovascular medicine (Fig. 1). To meet the needs of evolving disease epidemiology and evolving therapeutic diversity, imaging tests today seek to provide quantitative measures of physiology (*7*), seek to go beyond physiology by interrogating specific biologic mechanisms (*8*), and seek to go beyond the heart as a single organ by systems-based analysis of the interaction between the heart and other organs and tissues (*9*). The future vision is that modern cardiovascular imaging will have a profound role in providing highly effective biomarkers for personalized guidance of modern systems-based and targeted cardiovascular therapy (*10*). The molecular specificity and quantitative potential of radionuclide-based imaging techniques hold great promise in this regard (*11*). Eventually, theranostic pairs will emerge in cardiology, with a molecular imaging test providing actionable information for a matched, specific therapeutic intervention in a manner similar to concurrent approaches in oncology and to upcoming approaches in neurology and immunology (*12*).

This supplement of *The Journal of Nuclear Medicine* seeks to highlight the exciting new developments and opportunities for nuclear cardiology in the modern era of personalized cardiovascular medicine (Table 1). Di Carli shows how absolute quantification, tracers with superior kinetic properties, and integration with CT promote a transition from SPECT to PET for myocardial perfusion imaging and will therefore refine the workup of ischemic heart

Received Oct. 11, 2023; accepted Oct. 12, 2023.
For correspondence or reprints, contact Frank M. Bengel (bengel.frank@mh-hannover.de).
Published online Nov. 1, 2023.

DOI: 10.2967/jnumed.123.266845

TABLE 1
Evolution of Nuclear Cardiology

Going beyond …	Toward …
Relative regional perfusion	Absolute myocardial blood flow (*13*)
Single-organ analysis (heart)	Holistic approach (total body) (*14*)
Detection of cardiac involvement in systemic disease	Quantification of treatment effects (*15*)
Detection of cardiotoxicity of antitumor therapy	Systems-based approach toward tumor–heart crosstalk (*16*)
Gross visualization of cardiac inflammation	Dissection of specific immune mechanisms as precursors of remodeling (*17*)
Detection of late contractile failure	Quantification of early fibrotic activity (*18*)
Host response to infection	Direct detection of pathogens (*19*)
SPECT	PET (*13–19*)
Single modality	Multimodality approach (*13–19*)
Diagnosis of disease	Biomarkers for guidance of therapy (*13–19*)

disease (*13*). Knuuti et al. then show how the principle of quantitative blood flow imaging can be taken beyond the heart to look at total-body perfusion and systemic organ interaction, by use of novel PET systems with a large axial field of view (*14*). Modern tracers will also enable the concomitant assessment of extracardiac disease burden and cardiac involvement in systemic disease. This is exemplified by Dorbala et al. (*15*) in amyloidosis, for which novel, highly effective molecular therapies have been developed, and by Kersting et al. (*16*) in oncology, in which the continued success of targeted therapy leads to an increasing number of surviving patients entering chronic disease states, and in which effects on cardiac health become increasingly important, promoting the subdiscipline of cardiooncology. Finally, there is increasing attention toward the role of the immune system, fibrosis, and bacterial pathogens in cardiovascular disease. Here, novel tracers may again open avenues for molecular cardiac imaging toward applications in guidance of targeted therapy, as highlighted by Thackeray et al. for immunocardiology (*17*), by Bengel et al. for cardiac fibrosis (*18*), and by Roll et al. for cardiac infection (*19*).

Of note, this supplement has been specifically dedicated to imaging of the myocardium as the target that is most readily visualized by molecular imaging. Valvular (*20*) and vessel wall (*21*,*22*) pathologies have been reviewed separately recently and provide additional opportunities that will broaden the future of cardiovascular nuclear imaging even further.

As the coordinators of this supplement, we hope that you will enjoy reading it and that it will serve as a stimulus for expansion of clinical efforts, adoption of novel techniques, and design of innovative research in this exciting field.

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