Hellenic Journal of Cardiology (2016) xx, 1–5

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.journals.elsevier.com/hellenic-journal-of-cardiology/

REVIEW ARTICLE

The Role of Interventional Cardiology to Our Understanding of Basic Mechanisms Related to Coronary Atherosclerosis: "Thinking outside the box"

Konstantinos Dean Boudoulas, MD [a,*], Christodoulos Stefanadis, MD [b], Harisios Boudoulas, MD, Dr. [c,d], Hon, Dr. [c,d]

[a] *Associate Professor of Medicine/Cardiovascular Medicine, Division of Cardiovascular Medicine, Section of Interventional Cardiology, The Ohio State University, Columbus, Ohio, USA*
[b] *Professor of Cardiology, University of Athens (emeritus), Athens, Greece*
[c] *Professor of Medicine/Cardiovascular Medicine and Pharmacy (emeritus), The Ohio State University, Columbus, Ohio, USA*
[d] *Honorary Professor, Academician (an. mem.), Aristotle University of Thessaloniki, Thessaloniki, Greece*

Received 23 September 2016; received in revised form 30 September 2016; accepted 10 October 2016

KEYWORDS
interventional cardiology;
atherosclerosis

Abstract Interventional cardiology has contributed significantly to our understanding of coronary atherosclerosis. Interventional cardiology has allowed a correlation between the clinical picture of coronary atherosclerosis with the underlying pathology and has helped establish the evolution of atherosclerotic plaques *in vivo*. Better understanding of the basic mechanisms of coronary atherosclerosis, due to the contributions of interventional cardiology, will help cure and/or prevent coronary atherosclerosis in the next few decades. In this mini review, several of the remarkable contributions of interventional cardiology, which have allowed a better understanding of the pathophysiologic mechanisms related to coronary atherosclerosis, will be emphasized. In addition, certain projections for the future will be made based on current knowledge.

* Corresponding author. Konstantinos Dean Boudoulas, MD, Associate Professor of Medicine/Cardiovascular Medicine, Director, Interventional Cardiology Fellowship Program, Associate Director, Cardiac Catheterization Laboratory, The Ohio State University, Division of Cardiovascular Medicine, 473 W. 12th Avenue, Suite 200, Columbus, Ohio 43210, USA. Tel.: +1 614 293 7885; fax: +1 614 247 7789.
E-mail address: kdboudoulas@osumc.edu (K.D. Boudoulas).
Peer review under responsibility of Hellenic Cardiological Society.

http://dx.doi.org/10.1016/j.hjc.2016.10.002

1. Introduction

Several decades ago, it was almost impossible to even dream about the progress that has occurred in the diagnosis and management of coronary atherosclerosis.[1,2] Information available related to coronary atherosclerosis in the late fifties and early sixties were in its infancy. In 1768, Dr. Heberden described extremely well the clinical picture of angina pectoris at the Royal College of Physicians, however, the cause of chest pain was unknown at the time.[3] In 1912, Dr. Herrick presented for the first time at the Association of American Physicians in Chicago that an occlusion of a coronary artery could produce an acute myocardial infarction and not only death, which was the concept at that time.[4] In the middle of the last century, patients with an acute myocardial infarction had to stay on bed rest for almost forty days. At that time, Samuel Levine in Boston introduced a revolutionary concept that a patient with an acute myocardial infarction could sit in a chair.[2] In the mid 1950's, the president of the United States of America, Dwight D Eisenhower, had an acute myocardial infarction in Colorado and was forced to stay there for several weeks.[2] Obviously, our approach to patients with acute myocardial infarction is quite different today. The underlying pathology of coronary atherosclerosis can be defined with a great degree of accuracy in the cardiac catheterization laboratory. This diagnosis was difficult to achieve even at autopsy 60 years ago. Moreover, the development of percutaneous coronary interventions has allowed the revascularization of almost all coronary artery stenoses, including total occlusions, in patients with stable disease and/or acute coronary syndromes. These remarkable achievements have allowed clinicians to take better care of their patients and physicians/scientists to better understand the underlying pathophysiologic mechanisms of the disease. The discoveries related to the basic pathophysiologic mechanisms of atherosclerosis will help win the war against coronary atherosclerosis, which in turn will diminish or eliminate the role of interventional cardiology in this disease.[5–7] The focus of this paper will be to emphasize several of the remarkable achievements interventional cardiology has had on the underlying pathophysiologic mechanisms of atherosclerosis. The authors, who are both cardiologists and physicians/scientists with a special interest in translational research, will also make certain projections for the future based on current available information.

2. Correlation of Clinical Picture with Underlying Pathology and Pathophysiology

Prior to the introduction of coronary arteriography in clinical practice, it was impossible to correlate the clinical picture *in vivo* with the underlying coronary pathology. Dr Mason Sones in Cleveland Clinic in October 30, 1958, "accidentally" did a selective injection into the right coronary artery. To his surprise, the patient did not have any long-lasting serious issues after the injection. This was the beginning of a long journey that among others provided an *in vivo* correlation between the clinical picture of coronary atherosclerosis with the underlying pathology.[8] A few years later, a group of patients with chest pain and normal coronary arteries, the so-called "syndrome X", was described. Thus, it became obvious that not all chest pains are related to obstructive coronary artery disease.[1] Several decades later, several investigators reported that mild to moderate coronary artery stenosis is responsible for most myocardial infarctions[9,10]; this concept was against the conventional wisdom of the time. These observations challenged the concept that the diagnosis of coronary atherosclerosis could be based on stress-induced ischemia. Ischemia cannot be induced when the stenosis is less than 70% and thus, a stenosis that may produce a myocardial infarction or sudden cardiac death in certain instances cannot be diagnosed prior to a catastrophic event.[1] This information has stimulated the development of newer diagnostic techniques such as computed tomography, fractional flow reserve, and others, for the diagnosis of anatomic and physiologic significant coronary artery stenoses.[1,11–14] Although it was known that coronary artery bypass surgery may damage nerves also relieving chest pain and the incidence of angina, it was coronary angioplasty that directly demonstrated the association of chest pain with coronary artery stenosis when Andreas Gruenzing performed a coronary angioplasty in a patient with a critical left anterior coronary artery stenosis in September 26, 1977.[15] A decade later, Dr. Sigwart showed that placement of a stent after angioplasty decreased the incidence of restenosis. Other investigators later introduced the idea of covered stents and drug eluting stents. The introduction of stents, which may thrombosis, has stimulated research related to thrombosis and antithrombotic therapy.[1,16]

3. Thrombus Formation is Responsible for ST-Elevation Myocardial Infarction

Another major contribution of interventional cardiology was the concept that thrombus was almost always present in patients with a ST-elevation myocardial infarction (STEMI). Although pathologists earlier believed that thrombosis was responsible for a STEMI,[17] a prominent pathologists in the 1970's thought that thrombus formation within the coronary artery in patients with a STEMI was a post-mortem phenomena.[18] Obviously, this concept had a significant negative impact in the treatment of patients with an acute myocardial infarction for a substantial period of time. It was Dr. Dewood in 1980, almost a decade later, which proved *in vivo* that this concept was inaccurate.[19] He and his colleagues performed a coronary arteriography in patients with STEMI and demonstrated that within the first hours after the onset of chest pain thrombus was present in almost in all patients; 16 to 24 hours later, thrombus was seen only in the minority of these patients. It should be mentioned that coronary arteriography was absolutely contraindicated in patients with acute myocardial infarction in 1980. Immediately after this information, other investigators demonstrated that intracoronary injection of streptokinase produced dissolution of thrombus that resulted in a decreased in the size of myocardial necrosis.[20] These studies had a significant impact in our understanding of the pathogenesis of acute myocardial infarction and

Please cite this article in press as: Boudoulas KD, et al., The Role of Interventional Cardiology to Our Understanding of Basic Mechanisms Related to Coronary Atherosclerosis: "Thinking outside the box", Hellenic Journal of Cardiology (2016), http://dx.doi.org/10.1016/j.hjc.2016.10.002