Asymptomatic Atherosclerosis

Pathophysiology, Detection and Treatment

Edited by

Morteza Naghavi, MD
Society for Heart Attack Prevention and Eradication (SHAPE)
Houston, Texas
USA
Dedications and Acknowledgments

They say that dedicating a book is one of the most exquisite acts of love and generosity one can perform. I would agree, and would like to dedicate my efforts in realizing this book to the following:

To my father, Mohsen Naghavi, who grew up in a hardworking farmer family with 13 children who were fighting poverty and did not have the luxury of going to school. Nonetheless, he always inspired his children with stories of successful people and encouraged them to have great ambitions. He lived a difficult life as a bus driver, but brought up his 7 children to be thriving doctors, engineers, and teachers.

To my mother, Khadijeh Naghavi, whose countless sacrifices and never-ending patience have kept our family warm with love.

To my first mentors, Drs S. Ward Casscells and James T. Willerson, whose integrity and ingenuity taught me priceless lessons and enabled me to realize my “American Dream”.

To my respectful advisors, Drs P.K. Shah and Valentin Fuster whose generous support further helped me establish my career.

To my academic colleagues, Drs Erling Falk, Harvey Hecht, Mathew Budoff, Craig Hartley, Ralph Metcalfe, and Ioannis Kakadiaris for their friendship, trust and continued support.

To my collaborators at SHAPE, especially Dr. Khurram Nasir for editorial assistance, Dr. Khawar Gul and Lisa Brown for management assistance, Mark Johnson for graphic illustrations and Princess Fazon for administrative support, whose work made this book possible.

To my past and present associates, especially those I have not had a chance to thank and express my heartfelt appreciation.

And to you who will somehow be inspired by this book and its mission to eradicate heart attacks; you will become an important link in the long causal chain of heart attack eradication. Do not doubt the cause; our mission is truly achievable.

Cheers to a heart attack-free future for mankind!

Houston, TX

Morteza Naghavi, MD
Preface

In the past century, preventive cardiology has been in a defensive mode. Since James Herrick first reported Clinical Features of Sudden Obstruction of the Coronary Artery Disease in JAMA 1912, and Paul Dudley White wrote the textbook of Heart Disease in 1930 and helped create cardiac care units, cardiovascular medicine for the most part has focused on the detection and treatment of symptomatic coronary artery disease. Although Dr. White recognized the importance of preventive cardiology by championing the Framingham Heart Study and establishing the American Heart Association, his dream of “mastering presenile atherosclerosis” is still unrealized. Over the past 50 years, the Framingham study defined the traditional cardiovascular risk factors of smoking, high serum cholesterol, high blood pressure, diabetes and lack of exercise, and the American Heart Association raised public awareness for early detection and treatment of these risk factors. However, atherosclerotic cardiovascular disease has remained the number one killer, diabetes and obesity have wildly increased, and out-of-hospital sudden cardiac deaths is still high and is increasing in women.

New multipronged preventive strategies must be adopted to address these failures, beginning with a change in mindset from a passive defensive to an active offensive mode. The war against sudden coronary death must be shifted from hospitals to homes, and from advanced cardiac care units to primary care offices. In making such a shift, we must walk the walk, as we talk the talk. Attention must shift from the less effective and more expensive treatment of symptomatic atherosclerosis to the early detection and aggressive treatment of asymptomatic atherosclerosis.

Existing risk factor based stratifications e.g., the Framingham Risk Score, have proven grossly inadequate, particularly in identifying the vulnerable patients who are at risk of a near term future event. The traditional methods must be replaced with the more accurate, yet underutilized, measures of subclinical atherosclerosis, notably coronary artery calcium scanning and carotid intima-media thickness measurement. Treatment of asymptomatic patients must be based on the severity of atherosclerosis regardless of the risk factors. The SHAPE initiative is an effort to move in this direction.

In this book, leading cardiovascular physicians and investigators present the latest developments that illuminate the path to translating Dr. White’s dream into reality. We must, and I believe we can, master asymptomatic atherosclerosis to accomplish the mission of eradicating heart attacks in the twenty-first century.

Houston, TX

Morteza Naghavi, MD
Foreword

Since the landmark Framingham Heart Study introduced the concept of cardiovascular risk factors 50 years ago, the prediction and prevention of adverse cardiac events have been based primarily on the identification and treatment of these risk factors. Nonetheless, cardiovascular disease has remained the primary cause of mortality and morbidity in developed countries, and is rapidly increasing in the developing world. It is now obvious that new strategies, in addition to the traditional methods, are needed to fight the growing epidemic of atherosclerotic cardiovascular disease. In my view, early detection and treatment of high-risk asymptomatic atherosclerosis is a leading candidate to fulfill that role.

I would like to congratulate Dr. Naghavi and colleagues at the Society for Heart Attack Prevention and Eradication (SHAPE) for their pioneering efforts to advance the early detection and treatment of asymptomatic atherosclerosis. Despite the many challenges ahead, this is a worthy and timely effort that goes beyond traditional risk assessment, and has the potential to transform preventive cardiology. The driving passion and commitment of the members of the SHAPE Task Force is commendable; it serves as an example to all of us who are devoted to eradicating the epidemic of atherosclerotic cardiovascular disease particularly sudden heart attacks and strokes.

I am delighted to welcome “Asymptomatic Atherosclerosis” and look forward to its positive impacts on improving the knowledge and practice of preventive cardiology.

Valentin Fuster, M.D., Ph.D.
Director of the Cardiovascular Institute and Center for Cardiovascular Health
Mount Sinai Medical Center – New York, NY
President of the World Heart Federation
Past President of the American Heart Association
## Contents

Preface ........................................................................................................................................ vii  
Foreword ................................................................................................................................... ix  
Contributors ............................................................................................................................... xvii  

1 Preventive Cardiology: The SHAPE of the Future................................................................. 1  
   *Morteza Naghavi*  

2 From Vulnerable Plaque to Vulnerable Patient................................................................. 13  
   *Morteza Naghavi and Erling Falk*  

3 Pathology of Vulnerability Caused by High-Risk (Vulnerable) Arteries and Plaques .......... 39  
   *Troels Thim, Mette Kallestrup Hagensen, Jacob Fog Bentzon, and Erling Falk*  

4 Pathophysiology of Vulnerability Caused by Thrombogenic (Vulnerable) Blood .......... 53  
   *Giovanni Cimmino, Borja Ibanez, and Juan Jose Badimon*  

5 Vulnerability Caused by Arrhythmogenic Vulnerable Myocardium................................ 67  
   *Ariel Roguin*  

6 Approach to Atherosclerosis as a Disease: Primary Prevention Based on the Detection  
   and Treatment of Asymptomatic Atherosclerosis .............................................................. 77  
   *Morteza Naghavi, Erling Falk, Khurram Nasir, Harvey S. Hecht, Matthew J. Budoff,  
     Zahi A. Fayad, Daniel S. Berman, and Prediman K. Shah*  

**SECTION I RISK FACTORS AND CIRCULATING MARKERS OF ASYMPTOMATIC  
ATHEROSCLEROTIC CARDIOVASCULAR DISEASE**  

7 History of the Evolution of Cardiovascular Risk Factors and the Predictive  
   Value of Traditional Risk-Factor-Based Risk Assessment ................................................ 89  
   *Amit Khera*  

8 Comprehensive Lipid Profiling Beyond LDL ................................................................. 107  
   *Benoit J. Arsenault, S. Matthijs Boekholdt, John J.P. Kastelein,  
     and Jean-Pierre Després*  

9 New Blood Biomarkers of Inflammation and Atherosclerosis ....................................... 119  
   *Natalie Khuseyinova and Wolfgang Koenig*  

10 Genomics and Proteomics: The Role of Contemporary Biomolecular Analysis  
    in Advancing the Knowledge of Atherosclerotic Coronary Artery Disease .................. 135  
   *Gary P. Foster and Naser Ahmadi*  

11 Circulating Endothelial Progenitor Cells: Mechanisms and Measurements .................. 151  
   *Jonathan R. Murrow and Arshed A. Quyyumi*  

xi
12 Family History: An Index of Genetic and Environmental Predisposition to Coronary Artery Disease ........................................................................................................ 169
   Shivda Pandey and Khurram Nasir

13 Endothelial Activation Markers in Sub-clinical Atherosclerosis: Insights from Mechanism-Based Paradigms ............................................................................ 179
   Victoria L.M. Herrera and Joseph A. Vita

SECTION II  NON INVASIVE, NON IMAGING, ASSESSMENT OF ASYMPTOMATIC Atherosclerotic Cardiovascular Disease

14 Exercise Stress Testing in Asymptomatic Individuals and Its Relation to Subclinical Atherosclerotic Cardiovascular Disease ......................................................... 197
   Kevin S. Heffernan

15 The Ankle Brachial Index ........................................................................................................ 211
   Matthew A. Allison and Mary M. McDermott

16 Arterial Elasticity/Stiffness .................................................................................................. 225
   Daniel A. Duprez and Jay N. Cohn

17 Assessment of Endothelial Function in Clinical Practice .................................................. 237
   Jeffrey T. Kuvin

18 Digital (Fingertip) Thermal Monitoring of Vascular Function: A Novel, Noninvasive, Nonimaging Test to Improve Traditional Cardiovascular Risk Assessment and Monitoring of Response to Treatments .................................................. 247

19 Assessment of Macro- and Microvascular Function and Reactivity ..................................... 265
   Craig J. Hartley and Hirofumi Tanaka

SECTION III  NON INVASIVE STRUCTURAL IMAGING OF ASYMPTOMATIC Atherosclerotic Cardiovascular Disease

20 Coronary Artery Calcium Imaging ...................................................................................... 279
   Harvey S. Hecht

21 Noninvasive Ultrasound Imaging of Carotid Intima Thickness .......................................... 285
   Tasneem Z. Naqvi

22 Carotid Intima-Media Thickness: Clinical Implementation in Individual Cardiovascular Risk Assessment ................................................................................. 319
   Ward A. Riley

23 Computed Tomographic Angiography .................................................................................. 323
   Harvey S. Hecht

24 Role of Noninvasive Imaging using CT for Detection and Quantitation of Coronary Atherosclerosis ......................................................................................... 335
   John A. Rumberger
25 Noninvasive Coronary Plaque Characterization: CT Versus MRI ........................................ 351
   John A. Rumberger
26 Magnetic Resonance Imaging .......................................................................................... 357
   Zahi A. Fayad
27 The Role of MRI in Examining Subclinical Carotid Plaque ........................................... 363
   Chun Yuan, Hideki Ota, Xihai Zhao, and Tom Hatsukami
28 Comprehensive Non-contrast CT Imaging of the Vulnerable Patient ................................. 375
   Damini Dey, Ioannis A. Kakadiaris, Matthew J. Budoff, Morteza Naghavi,
   and Daniel S. Berman

SECTION IV  NON INVASIVE FUNCTIONAL IMAGING OF ASYMPTOMATIC
ATHEROSCLEROTIC CARDIOVASCULAR DISEASE

29 Ultrasound Assessment of Brachial Artery Reactivity ..................................................... 395
   A. Rauoof Malik and Iftikhar J. Kullo
30 Cardiac Imaging for Ischemia in Asymptomatic Patients: Use of Coronary Artery
   Calcium Scanning to Improve Patient Selection: Lessons from the EISNER Study .......... 411
   Alan Rozanski, Heidi Gransar, Nathan D. Wong, Leslee J. Shaw, Michael J. Zellweger,
   and Daniel S. Berman
31 Targeted MRI of Molecular Components in Atherosclerotic Plaque ................................ 429
   Zahi A. Fayad
32 Noninvasive Imaging of the Vulnerable Myocardium: Cardiac MRI and CT Based.......... 433
   Ricardo C. Cury, Anand Soni, and Ron Blankstein

SECTION V  INVASIVE (INTRAVASCULAR) RISK STRATIFICATION FOR DETECTION OF
VULNERABLE (HIGH-RISK) ASYMPTOMATIC Atherosclerotic Plaques

33 Angiography for Detection of Complex and Vulnerable Atherosclerotic Plaque ............... 455
   James A. Goldstein
34 Intravascular Characterization of Vulnerable Coronary Plaque ....................................... 461
   James A. Goldstein and James E. Muller
35 Detecting Vulnerable Plaque Using Invasive Methods .................................................... 475
   Robert S. Schwartz and Arturo G. Touchard
36 Assessment of Plaque Burden and Plaque Composition Using Intravascular Ultrasound ..... 483
   Paul Schoenhagen, Anuja Nair, Stephen Nicholls, and Geoffrey Vince
37 Vulnerable Anatomy; The Role of Coronary Anatomy and Endothelial Shear Stress in the
   Progression and Vulnerability of Coronary Artery Lesions: Is Anatomy Destiny? ............ 495
   Charles L. Feldman, Yiannis S. Chatzizisis, Ahmet U. Coskun,
   Konstantinos C. Koskinas, Morteza Naghavi, and Peter H. Stone
38 Vasa Vasorum Imaging ................................................................................................... 507
   Ioannis A. Kakadiaris, Sean O’Malley, Manolis Vavaranakis, Ralph Metcalfe,
   Craig J. Hartley, Erling Falk, and Morteza Naghavi
SECTION VI  SCREENING FOR RISK ASSESSMENT OF ASYMPTOMATIC AT-RISK POPULATION AND IDENTIFICATION OF THE VULNERABLE PATIENT – THE SHAPE PARADIGM

39  From Vulnerable Plaque to Vulnerable Patient – Part III ........................................................... 517

40  Cost Effectiveness of Screening Atherosclerosis ............................................................... 537
Leslee J. Shaw and Ron Blankenstein

41  Monitoring of Subclinical Atherosclerotic Disease............................................................... 549
Daming Zhu, Allen J. Taylor, and Todd C. Villines

42  Implications of SHAPE Guideline for Improving Patient Compliance.............................. 569
Matthew J. Budoff

43  The SHAPE Guideline: Why Primary Care Physicians Should Embrace It .................. 577
Robert A. Mendes

44  Should We Treat According to the SHAPE Guidelines?.................................................... 581
Paolo Raggi and Stamatios Lerakis

45  Duty-Bound: Rational Foundations of Clinical Strategies for Prevention of Cardiovascular Events ........................................................................................................... 587
George A. Diamond and Sanjay Kaul

46  A Time to Live: Dynamic Changes in Risk as the Basis for Therapeutic Triage.............. 597
Sanjay Kaul and George A. Diamond

SECTION VII  TREATMENT OF ASYMPTOMATIC Atherosclerotic CardioVascular Disease and the Vulnerable Patients: Systemic Therapies

47  LDL Targeted Therapies ......................................................................................................... 605
Raul D. Santos, Khurram Nasir, and Roger S. Blumenthal

48  Antioxidants as Targeted Therapy: A Special Protective Role for Pomegranate and Paraoxonases (PONs) ................................................................................................................... 621
Mira Rosenblat and Michael Aviram

49  The Multiconstituent Cardiovascular Pill (MCCP): Challenges and Promises of Population Based Prophylactic Drug Therapy for Heart Attack Prevention and Eradication ............................................................................................................. 635
Michael J. Jamieson, Harvey S. Hecht, and Morteza Naghavi

50  Vaccine for Atherosclerosis: An Emerging New Paradigm ............................................ 649
Prediman K. Shah, Kuang-Yuh Chyu, Jan Nilsson, and Gunilla N. Fredrikson
SECTION VIII  LOCAL AND FOCAL THERAPIES FOR STABILIZATION OF VULNERABLE ARTERIES AND PLAQUES

51 Drug-Eluting Stents: A Potential Preemptive Treatment Choice for Vulnerable Coronary Plaques ................................................................. 661
   Edwin Lee, George Dangas, and Roxana Mehran

52 Intrapericardial Approach for Pancoronary Stabilization of the Vulnerable Arteries and Myocardium ........................................................... 671
   Venkatesan Vidi and Sergio Waxman

SECTION IX  EDUCATIONS, LIFE STYLE MODIFICATIONS AND NON-PHARMACOLOGIC TREATMENTS FOR PRIMARY PREVENTION AND SAVING THE VULNERABLE

53 Dietary Management for Coronary Atherosclerosis Prevention and Treatment .................. 689
   Michel de Lorgeril and Patricia Salen

54 Management of Preconditioning Physical Activity in a Vulnerable Patient:
   Getting in SHAPE ............................................................................................ 699
   Sae Young Jae

55 Last Chance for Prevention (Acute Prevention): Identification
   of Prodromal Symptoms and Early Heart Attack Care ...................................... 707
   Raymond D. Bahr, Yasmin S. Hamirani, and Morteza Naghavi

Index .................................................................................................................. 723
Contributors

Naser Ahmadi, MD • Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA, USA

Matthew A. Allison, MD • Department of Family and Preventive Medicine, Moores Cancer Center, University of California San Diego, La Jolla, CA, USA

Dan Arking, PhD • McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Benoit J. Arsenault, MSc • Department of Anatomy and Physiology, Université Laval, Quebec, QC, Canada

Michael Aviram, DSc • Technion Institute of Technology, Rappaport Faculty of Medicine, Haifa, Israel

Juan Jose Badimon, PhD • Cardiovascular Biology Research Laboratory, Cardiovascular Institute, Mount Sinai School of Medicine, New York, NY, USA

Raymond D. Bahr, MD, FACC • St. Agnes Healthcare, Baltimore, MD, USA

Jacob Fog Bentzon, MD, PhD • Department of Cardiology, Research Unit, Aarhus University Hospital, Aarhus, Denmark

Daniel S. Berman, MD • Department of Cardiac Imaging and Nuclear Cardiology, Cedars-Sinai Medical School, Los Angeles, CA, USA

Ron Blankstein, MD • Department of Radiology, Cardiac MRI-PET-CT Program, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

Roger S. Blumenthal, MD • Preventive Cardiology Center, Johns Hopkins Hospital, Baltimore, MD, USA

S. Matthijs Boekholdt, MD • Department of Vascular Medicine, Academic Medical Center, Amsterdam, The Netherlands

Matthew J. Budoff, MD • BioMed CT Reading Center, Harbor-UCLA Medical Center, Torrance, CA, USA

Mercedes R. Carnethon, PhD • Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Yiannis S. Chatzizisis • Cardiovascular Division, Brigham and Women’s Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115

Kuang-Yuh Chyu, MD, PhD • Division of Cardiology, Cedars-Sinai Medical Center, Los Angeles, CA, USA

Giovanni Cimmino, MD • Cardiovascular Biology Research Laboratory, Cardiovascular Institute, Mount-Sinai School of Medicine, New York, NY, USA
Contributors

Jay N. Cohn, MD • Division of Cardiology, Department of Medicine, University of Minnesota Medical Center, Minneapolis, MN, USA

Ahmet U. Coskun • Cardiovascular Division, Brigham and Women’s Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115

Ricardo C. Cury, MD • Department of Radiology, Cardiac MRI-PET-CT Program, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

George Dangas, MD, PhD • Center for Interventional Vascular Therapy, Columbia University Medical Center and New York Presbyterian Hospital, New York, NY, USA

Jasenka Demirovic, MD, MSc, PhD • Division of Epidemiology, School of Public Health, The University of Texas Health Science Center, Houston, TX, USA

Damini Dey, PhD • Department of Imaging, Cedars-Sinai Medical Center, Los Angeles, CA, USA

Jean-Pierre Després, PhD, FAHA • Québec Heart Institute, Montreal, Quebec, QC, Canada

George A. Diamond, MD • Division of Cardiology, Cedars-Sinai Medical Center, Los Angeles, CA, USA

Pamela S. Douglas, MD, FACC • Cardiovascular Imaging Center, Duke University Medical Center, Durham, NC, USA

Daniel A. Duprez, MD, PhD • Division of Cardiology, Department of Medicine, University of Minnesota Medical Center, Minneapolis, MN, USA

Erling Falk, MD, PhD • Department of Cardiology Research, Aarhus University Hospital, Skejby, Aarhus, Denmark

Ole Faergeman, MD, MDSc • Section of Preventive Cardiology, Department of Medicine and Cardiology, Aarhus Amtssygehu University Hospital, Aarhus, Denmark

Zahi A. Fayad, PhD • Department of Radiology and Department of Cardiology, Mount-Sinai School of Medicine, New York, NY, USA

Charles L. Feldman • Cardiovascular Division, Brigham and Women’s Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115

Gary P. Foster, MD • Texas Cardiovascular Consultants, P.A., Austin, TX, USA

Gunilla N. Fredrikson, PHD • Department of Medicine, University Hospital MAS, Malmo, Sweden

James A. Goldstein, MD • Division of Cardiology, William Beaumont Hospital, Royal Oak, MI, USA

Heidi Gransar, MS • Departments of Imaging and Medicine and the Burns and Allen Research Institute, Cedars-Sinai Medical Center and the Department of Medicine, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, CA, USA

Mette Kallestrup Hagensen, MSc • Department of Zoophysiology, Institute of Biological Sciences, University of Aarhus, Aarhus, Denmark

Yasmin S. Hamirani, MD • St. Agnes Healthcare, Baltimore, MD, USA
CRAIG J. HARTLEY, PHD • Department of Medicine, Section of Cardiovascular Sciences, Baylor College of Medicine, Houston, TX, USA

TOM HATSKUAMI, MD • Department of Radiology, Vascular Imaging Lab, University of Washington, Seattle, WA, USA

HARVEY S. HECHT, MD • Department of Interventional Cardiology, Lenox Hill Hospital, New York, NY, USA

KEVIN S. HEFFERNAN, PhD • Department of Kinesiology/Exercise Physiology, University of Illinois at Urbana-Champaign, Urbana, IL, USA

VICTORIA L.M. HERRERA, MD • Department of Medicine, Section of Molecular Medicine, Boston University School of Medicine, Boston, MA, USA

BORJA IBANEZ, MD • Cardiovascular Biology Research Laboratory, Cardiovascular Institute, Mount-Sinai School of Medicine, New York, NY, USA

SAE YOUNG JAE, PhD • The Health and Integrative Physiology Laboratory, Department of Sports Informatics, University of Seoul, Seoul, South Korea

CRAIG JAMIESON • Endothelix Inc., Houston, TX, USA

MICHAEL J. JAMIESON, MD • Senior Director, RMRS Cardiovascular, Pfizer Inc., Houston, TX, USA

K.E. JUHANI AIRAKSINEN, MD • Cardiovascular Laboratory, Department of Medicine, University of Turku, Turku, Finland

IOANNIS A. KAKADIARIS, PhD • Department of Engineering, University of Houston, Houston, TX, USA

JOHN J.P. KASTELEIN, MD, PhD • Academic Medical Center, Amsterdam, The Netherlands

SANJAY KAUL, MD • Division of Cardiology, Cedars-Sinai Medical Center, Los Angeles, CA, USA

MORTON KERN, MD • Division of Cardiology, Department of Medicine, University of California at Irvine, Orange, CA, USA

AMIT KHERA, MD, MSc • Division of Cardiology, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, USA

NATALIE KHUSEYINOVA, MD • Department of Internal Medicine, Cardiology, University of Ulm Medical Center, Ulm, Germany

WOLFGANG KOENIG, MD, PhD • Department of Internal Medicine, Cardiology, University of Ulm Medical Center, Ulm, Germany

KONSTANTINOS C. KOSKINAS • Cardiovascular Division, Brigham and Women’s Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115

IFTIKAR J. KULLO, MD • Department of Cardiovascular Disease, Gonda Vascular Center, Mayo Clinic, Rochester, MN, USA

JEFFREY T. KUVIN, MD • Cardiovascular Imaging and Hemodynamics Laboratory, Tufts Medical Center, Boston, MA, USA

EDWIN LEE, MD, PhD • Center for Interventional Vascular Therapy, Columbia University Medical Center, New York, NY, USA
Contributors

Stamatios Lerakis, MD • Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA

Michel de Lorgeril, MD • Cardiovascular Stress and Associated Pathology Laboratory, Joseph Fourier University, Grenoble, France

A. Rauoof Malik, MD • Division of Cardiovascular Diseases, Mayo Clinic, Rochester, MN, USA

Mary M. McDermott, MD • Division of General Internal Medicine, Northwestern Medical Faculty Foundation, Chicago, IL, USA

Roxana Mehran, MD • Center for Interventional Vascular Therapy, Columbia University Medical Center, New York, NY, USA

Robert A. Mendes, MD • Division of Vascular Surgery, Department of Surgery, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Ralph Metcalfe, MD • Department of Mechanical Engineering, University of Houston, Houston, TX, USA

James E. Muller, MD • Department of Medicine, Cardiac Unit, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

Jonathon R. Murrow, MD • Division of Cardiology, Department of Internal Medicine, Emory University School of Medicine, Atlanta, GA, USA

Morteza Naghavi, MD • Society for Heart Attack Prevention and Eradication (SHAPE) 710 North Post Oak, Suite 400 Houston, Texas 77024

Anuja Nair, PhD • Department of Biomedical Engineering, Cleveland Clinic Foundation, Cleveland, OH, USA

Tasneem Z. Naqvi, MD • Department of Medicine, University of Southern California, Los Angeles, CA, USA

Khurram Nasir, MD • Cardiac MR-PET-CT Program, Massachusetts General Hospital and Department of Radiology, Harvard Medical School, Boston, MA, USA

Stephen Nicholls, MD, PhD • Department of Cardiovascular Medicine, Cleveland Clinic Foundation, Cleveland, OH, USA

Jan Nilsson, MD, PhD • Department of Medicine, University Hospital MAS, Malmo, Sweden

Sean O’Malley, MD • Department of Engineering, University of Houston, Houston, TX, USA

Hideki Ota, MD, PhD • Department of Radiology, Vascular Imaging Lab, University of Washington, Seattle, WA, USA

Shivda Pandey, MD • Department of Radiology, Cardiac MRI-PET-CT Program, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

Arshed A. Quyyumi, MD • Division of Cardiology, Department of Internal Medicine, Emory University School of Medicine, Atlanta, GA, USA

Paolo Raggi, MD • Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA
Ward A. Riley, PhD • Department of Neurology, Wake Forest University, Winston-Salem, NC, USA
Ariel Roguin, MD, PhD • Department of Cardiology, Rambam Medical Center, Haifa, Israel
Mira Rosenblat, MSc • Technion Institute of Technology, Rappaport Faculty of Medicine, Haifa, Israel
Alan Rozanski, MD • Department of Cardiology, St. Luke’s Roosevelt Hospital Center, New York, NY, USA
Yoram Rudy, PhD • Cardiac Bioelectricity and Arrhythmia Center, Washington University in St. Louis, St. Louis, MO, USA
John A. Rumberger, MD, PhD • The Princeton Longevity Center, Princeton, NJ, USA
Patricia Salen, BSc • Faculté de Médecine, Domaine de la Merci, Université de Grenoble, La Tronche, France
Raul D. Santos, MD • Cardiovascular Specialists, P.A., Lewisville, TX, USA
Paul Schoenhagen, MD • Department of Diagnostic Radiology and Cardiovascular Medicine, Cleveland Clinic Foundation, Cleveland, OH, USA
Robert S. Schwartz, MD • Minneapolis Heart Institute and Abbott Northwestern Hospital, Minneapolis, MN, USA
Prediman K. Shah, MD • Director, Division of Cardiology and Atherosclerosis Research Center, Cedars-Sinai Medical Center, Los Angeles, CA, USA
Leslee J. Shaw, PhD • Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA
Anand Soni, MD • Department of Radiology, Cardiac MRI-PET-CT Program, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA
Peter H. Stone • Cardiovascular Division, Brigham and Women’s Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115
Hirofumi Tanaka, PhD • Department of Kinesiology and Health Education, The University of Texas at Austin, Austin, TX, USA
Allen J. Taylor, MD • United States Army Cardiology Service, Walter Reed Army Medical Center, Washington, DC, USA
Troels Thim, MD • Atherosclerosis Research Unit, Department of Cardiology, Aarhus University Hospital, Skejby, Aarhus, Denmark
Arturo G. Touchard, MD • Minneapolis Heart Institute, Minneapolis, MN, USA
Manolis Vavuranakis, MD • Department of Cardiology, Hippokration Hospital, Athens Medical School, Athens, Greece
Venkatesan Vidi, MD • Department of Cardiovascular Medicine, Lahey Clinic, Burlington, MA and Tufts University School of Medicine, Boston, MA, USA
Todd C. Villines, MD • United States Army Cardiology Service, Walter Reed Army Medical Center, Washington, DC, USA
Contributors

Geoffrey Vince, PhD • Department of Biomedical Engineering, Cleveland Clinic Foundation, Lerner Research Institute, Cleveland, OH, USA

Joseph A. Vita, MD • Department of Medicine, Section of Cardiovascular Medicine, Boston University School of Medicine, Boston, MA, USA

Sergio Waxman, MD • Department of Cardiovascular Medicine, Lahey Clinic, Burlington, MA and Tufts University School of Medicine, Boston, MA, USA

Nathan D. Wong, PhD, MPH • Heart Disease Prevention Program, University of California at Irvine, Irvine, CA, USA

Albert A. Yen, MD • Endothelix Inc., Houston, TX, USA

Chun Yuan, PhD • Department of Radiology, Vascular Imaging Lab, University of Washington, Seattle, WA, USA

Michael J. Zellweger, MD • Department of Cardiology, University Hospital, Basel Switzerland

Xihai Zhao, MD, PhD • Department of Radiology, Vascular Imaging Lab, University of Washington, Seattle, WA, USA

Daming Zhu, MD • Department of Internal Medicine, Johns Hopkins Bayview Medical Center, Baltimore, MD, USA
Preventive Cardiology: The SHAPE of the Future

Morteza Naghavi

Contents

Introduction
Traditional Preventive Cardiology
Modern Preventive Cardiology
The Big Picture: Health Care vs. Sick Care
Preventive Cardiology, Poorly Invested
Legislation for Prevention
Heart Attacks Can Be Eradicated
Conclusion
References

Abstract

In the twentieth century, atherosclerotic cardiovascular disease (ACVD) manifesting as a “heart attack,” has claimed millions of lives every year, and killed more people than all wars combined. An epidemic of this magnitude makes it very difficult to imagine a future in which heart attacks are eradicated. Nonetheless, the mission of eradicating heart attacks is no more challenging than the mission of landing humans on Mars. The vision for a heart attack-free future can become a reality in the twenty-first century and can significantly increase human life expectancy. This goal is achievable if we, including academia, industry, health-care providers, payers, and policymakers, invest in the detection and treatment of asymptomatic atherosclerotic as much as we have invested in the treatment of symptomatic atherosclerosis. Primary prevention of ACVD, through treatment of risk factors of atherosclerosis, public education, and promotion of heart-healthy life style, has been the main focus of cardiovascular organizations such as the American Heart Association. However, the continued overwhelming burden of ACVD and disappointing trends in the prevalence of ACVD risk factors, particularly obesity and diabetes, have made it clear that traditional methods are inadequate and new strategies are urgently needed. Recent discoveries have created paradigm shifts in our understanding of the underlying mechanisms of ACVD and the sequence of events that result in athero-thrombotic events. These scientific discoveries, along with new diagnostic and therapeutic developments, have opened the way to unprecedented opportunities including (1) screening for early detection and aggressive treatment of the “vulnerable patient” based on noninvasive imaging of asymptomatic atherosclerosis, (2) monitoring therapies and evaluating progression or regression of the disease based on structural, functional, and molecular markers of ACVD, (3) development of safe and
effective “Polypills” for preemptive population-based therapy, (4) development of safe and effective focal therapies, such as bio-absorbable drug-eluting stents, for rapid stabilization of the “vulnerable plaque,” and (5) immune modulation and vaccination strategies for prevention of atherosclerosis at an early age and halting its progression later in life. Simultaneously, the fast evolving IT and communication technologies, as well as low-cost home health-monitoring devices, will facilitate rapid dissemination of new information, empower consumers, and help shift cardiovascular care from hospitals to the home. Through the above, our modern preventive cardiology will shape the future and will lead to the eradication of heart attack in the twenty-first century.

**Key words:** Preventive cardiology; Asymptomatic atherosclerosis; Subclinical atherosclerosis; Primary prevention; Heart attack; Stroke, Coronary artery disease; Coronary heart disease; Carotid IMT – Carotid intima media thickness; Coronary calcium score; Vulnerable plaque; Vulnerable patient; Coronary risk assessment; Cardiovascular risk assessment; Healthcare policy; Atherosclerosis vaccination; PolyPill

**INTRODUCTION**

Atherosclerotic cardiovascular disease (ACVD), caused by ischemic complications of arterial atherosclerotic plaques manifested primarily through sudden cardiac death, acute coronary syndromes (ACS) and stroke, is the leading cause of death and disability in most developed countries, and is dramatically increasing in the developing nations. It is projected that by the year 2025 approximately 80–90% of all the cardiovascular diseases in the world will be occurring in low and middle income countries [1]. Despite many satisfactory statistical trends presented by the American Heart Association [2] and celebratory comments by opinion leaders [3] (as if we have conquered heart attacks), more Americans are dying from heart attacks now than they were 50-years ago. This statement is not true about polio and smallpox. While other areas of science and technology have witnessed incredible advances, ACVD and sudden cardiac death still kill apparently healthy people, and claim millions of lives and billions of dollars worldwide. Ironically, despite such a huge loss of lives and dollars every year, most cases of heart attacks and mortality or morbidity associated with ACVD can be prevented by early detection and aggressive treatment of asymptomatic atherosclerosis. Since 1960, a myriad of articles have been added to the medical literature offering insights into this major public health dilemma. However, a very unique opportunity to ease the dilemma, namely early detection and aggressive treatment of high-risk asymptomatic or presymptomatic atherosclerotic individuals (the vulnerable patients), has received little attention. It is well known that ACS do not occur without a preceding atherosclerotic plaque and that atherosclerosis remains hidden (asymptomatic) until too late (myocardial infarction and stroke) [4]. Nonetheless, very few efforts have focused on identification of the very high-risk (vulnerable) individuals with a high burden of asymptomatic atherosclerosis. Since 2003, this critical topic has been the focus of the SHAPE (Screening for Heart Attack Prevention and Education) Task Force and resulted in the establishment of the SHAPE organization (Society for Heart Attack Prevention and Eradication) [5–7]. The SHAPE initiative aims to advance ACVD risk assessment strategies in the asymptomatic population for saving the vulnerable patient, which current strategies have failed to accomplish.

**TRADITIONAL PREVENTIVE CARDIOLOGY**

Prevention of ACVD is categorized into primary prevention and secondary prevention. Primary prevention can be defined as the prevention of the first heart attack or stroke, while secondary prevention deals with the prevention of the second/recurrent heart attack or stroke. Neither the concept nor
the practice of primary prevention existed for ACVD prior to the 1950s when pioneering epidemiologists such as Ancel Key, Jerry and Rose Stamler, William Kannel, Henry Blackburn and others, reported convincing epidemiologic associations between high-fat diet, high serum cholesterol, high blood pressure, smoking, physical inactivity, etc. (termed “risk factors”) and ACVD. Despite major accomplishments in reducing the age-adjusted incidence of death from coronary heart disease and stroke (which is partially because of reduced case-fatality rate), the prevalence of ACVD and its associated morbidity, e.g., heart failure, have steadily increased in the past few decades. The incidence and prevalence of most risk factors (except for smoking) have increased or not changed. With the rapidly growing epidemic of obesity, the war against ACVD-prone life style is far from won, if not already lost. It is obvious that our society is facing a serious interruption in the chain of knowledge, attitude, and practice (KAP) to maintain a heart-healthy life (Fig. 1).

Over the past 50 years, great progress has been made in the early detection and management of risk factors as well as the diagnosis and treatment of symptomatic ACVD, particularly ACS. However, very little has been accomplished for asymptomatic ACVD, which accounts for the majority of sudden cardiac death, silent MI, and silent stroke. Unlike most cancers, ACVD remains asymptomatic (subclinical) for decades. Even though the majority of asymptomatic ACVD can be detected and treated, no screening test is currently approved by federal agencies and made available to physicians and patients. Current traditional risk factor-based assessment strategies have clearly proven to be insufficient. A recent report based on the Get with the Guidelines initiative of the American Heart Association which studied 136,905 patients hospitalized with the diagnosis of ACVD, has shockingly revealed the inadequacy of LDL-cholesterol, HDL-cholesterol, and triglyceride in identifying high-risk individuals. The report showed 77, 45.4, and 61.8% of the patients had normal LDL, HDL, and triglyceride, respectively (Fig. 2a–c) [8]. This study has strongly confirmed prior reports suggesting poor predictive value of traditional risk factors, in particular dislipidemia, and clearly highlighted the shortcoming of existing NCEP Guidelines (National Cholesterol Education Program) [9–12].

**Fig. 1.** Most people know that cardiovascular risk factors such as high-fat diet and lack of exercise increase their chance of having a future heart attack, but very few people follow a “heart-healthy” life style. Can heart attacks ever be eradicated by educational campaigns that the American Heart Association has focused on?
In addition to the need for improving risk assessment in asymptomatic individuals, accurate monitoring of the response to therapy in treated patients is essential for success in both primary and secondary prevention of ACVD. In summary, there are two major problems in cardiology; (1) inaccurate individualized assessment of cardiovascular risk as illustrated in Fig. 3 and (2) inadequate

**Fig. 1.2** (a) Of 136,905 patients hospitalized with CAD, 77% had normal LDL levels below 130 mg/dl. (b) Of 136,905 patients hospitalized with CAD, 45.4% had normal HDL levels above 40 mg/dl. (c) Of 136,905 patients hospitalized with CAD, 61.8% had normal triglyceride levels below 150 mg/dl.
monitoring of the vascular response to treatments as illustrated in Fig. 4. The time has come to adopt new paradigms, beyond traditional ACVD risk factors, to address both these issues.

In this book, leading investigators in the field of ACVD present a new strategy for risk assessment and reduction that is largely based on noninvasive screening for early detection of asymptomatic ACVD itself (subclinical atherosclerosis) rather than for its risk factors. The new strategy stratifies the asymptomatic population based on a screening pyramid in which the intensity of treatment is tailored to the severity of atherosclerosis.
MODERN PREVENTIVE CARDIOLOGY

In the era of Google, remote robotic surgery, sub-millimeter noninvasive imaging, and nanotech-enabled mass proteomic assays, having millions of people (many of whom are indeed health conscious) living with, but unaware of, a huge coronary plaque burden is tragic and simply unacceptable. Physicians and researchers are responsible for taking actions and for helping the medical community to take full advantage of new knowledge and technology to save lives particularly in the very productive segment of the society (<75 years). After all, if investment in seat belts and airbags (low in cost-effectiveness) with proper regulatory provisions can be sold to automobile makers and users, investments for prevention of the number one killer should be successful, and will save many more lives (Fig. 5).

While new tactics aimed at increasing KAP of heart-healthy life styles and reduction of risk factors at the population level are absolutely necessary, new strategies are urgently needed to prevent imminent catastrophic effects. The ultimate preventive strategies must be directed toward the different levels of primary prevention (i.e., prevention of atherosclerosis risk factors in the entire population, mass treatment of atherosclerosis in a smaller at-risk population, and preemptive prevention of events in further smaller presymptomatic population. The first SHAPE guideline is directed at the early detection and

Fig. 5. Screening for asymptomatic atherosclerosis is needed to prevent symptomatic (fatal and or costly) ACVD.
treatment of subclinical atherosclerosis and fills the gap in the existing guidelines. Implementing such strategies can be visualized in a pyramid approach with the primary prevention of atherosclerosis at the bottom and the primary prevention of events in the presymptomatic population at the top (Fig. 6).

**THE BIG PICTURE: HEALTH CARE VS. SICK CARE**

The United States “health-care system” is a misnomer, since most of our rapidly rising federal medical care (Medicare) budget is spent on “sick care,” i.e., treating existing disease rather than promoting health and preventing disease. In 2007, the USA spent $2.26 trillion on health care, or $7,439 per person, up from $2.1 trillion, or $7,026 per capita, the previous year. This expenditure is forecasted to grow 35% in the next 5 years [13]. Will this be matched by a 35% increase in disease reduction and life expectancy? Obviously no! What, exactly, are Americans paying for? The answer is not clear, but what is clear is that more and more is spent on expensive therapies for the treatment of diseases, most of which are preventable. While this problem remains a hot topic in the media and political arena, little has been done to provide a solution.

**PREVENTIVE CARDIOLOGY, POORLY INVESTED**

Investment in preventive health care must go far beyond general public recommendations to consume healthy foods, exercise, and avoid smoking. Although issuing educational guidelines and updating the food pyramid are needed, there is much more to be done for preventive health care to
reach its full capability. With the growing number of expensive modalities in the tertiary cardiovascular care arena (e.g., drug-eluting stents, cardiac resynchronization therapy, and left ventricular assist devices), the cardiovascular health-care budget is increasingly absorbed into an area with minimum opportunities for adding productive life years. While it is universally agreed that the opportunity for prevention of death and saving quality-adjusted life years (QALY) is far greater in primary than secondary prevention, it is disappointing to see less than 10% of the total cardiovascular care budget routed toward the field of primary prevention. An arsenal of rigorous cost-effectiveness objections and regulatory barriers are exercised against new paradigms in the primary prevention arena. The currently allocated budget for cardiovascular screening (one cholesterol and blood pressure test every 5 years) is woefully inadequate for prevention of the number one killer compared to the preventive screening tests reimbursed for cancer (Fig. 7). In cardiology, primary prevention encompassing decreasing risk factors and screening for and treating subclinical atherosclerosis, is under-invested compared to the less efficacious secondary prevention (Fig. 8).

LEGISLATION FOR PREVENTION

The regulatory bodies and governmental agencies play a central role in this shift. Once the entrepreneurs, businessmen, and, subsequently, the physicians and the entire medical industry realize the opportunity for high ROI (return on investment) in preventive care, a new path will be open to unprecedented progress in our public cardiovascular health care. This strategy, of course, would make sense for other areas of medicine as well. However, given the prevalence and abrupt and fatal nature of heart attack and stroke, such a shift is most needed in the field of preventive cardiology. Currently, preventive cardiovascular health-care strategies are predominantly based on general recommendations and guidelines for heart-healthy life styles. Unlike the treatment of symptomatic ACVD, in which innovative technologies are easily and increasingly adopted, in the primary prevention of ACVD the adoption of new methods and technologies has been extremely slow. This becomes obvious when comparing the number of companies exhibiting at preventive cardiology conferences vs. interventional

![Fig. 7. The current allocation of the US preventive screening budget for the number one killer (CVD) compared to the number two killer (cancer) is very disproportionate.](image-url)
cardiology or cardiovascular surgery meetings. Without creating new opportunities for business developments in the field of primary prevention, it will be hard for the field to grow and fulfill its promises. Attracting investment in free and capitalistic societies can only be successful if ROI is greater than competing business opportunities. Unfortunately, in cardiology practice and business today, ROI in the prevention of the first heart attack and associated sudden death is much lower than ROI in the prevention of chest pain after the first heart attack. Obviously, this investment paradigm is faulty, since primary prevention can save many more lives and results in more productivity by reducing premature death and disability. The SHAPE Task Force helped introduce the first of such legislative initiatives in the United States to Texas legislature. The Texas Heart Attack Preventive Screening Bill (HB1290), which was inspired by the SHAPE guidelines, passed the Senate and became law in Texas effective September 2009. The law mandates insurance coverage for noninvasive imaging of asymptomatic atherosclerosis in the Framingham Intermediate Risk population [14, 15].

Although passing the Texas Heart Attack Preventive Screening law is considered a monumental milestone on the way of shifting cardiovascular health care to primary prevention and has set the stage for other states to follow, it is far from adequate for the ultimate goal of eradicating heart attacks. Additional policy reforms, such as the following, must be seriously considered by the legislative and executive bodies to address the number one killer.

1. Provide more reimbursement incentives for preventive health-care technologies than at present.
2. Empower primary care physicians to utilize state-of-the-art preventive diagnostic technologies.
4. Give incentive and funding priorities through NIH, NSF, and other federal research funding agencies to fund proposals with innovative technologies focusing on primary prevention.
5. Empower consumers to take charge of their health by reducing regulatory (FDA) barriers for accessing safe and effective drugs such as statins (over-the-counter access).

Fig. 8. Comparing to the treatment of a heart attack, its prevention is woefully under-invested.
6. Give economic incentive (such as tax breaks) to the medical industry for any future products they bring to the market focusing on the primary prevention.

7. Give economic incentive (tax breaks) to at-risk populations to reduce their burden of CVD risk, e.g., weight loss, stop smoking cessation, cholesterol, and blood pressure lowering.

8. Increase the tax on smoking, both consumers and providers.

9. Shift cardiovascular prevention from the hospital and doctors’ offices to the home; give incentive to home health monitoring companies and reduce legal barriers for mass adoption of practicing telemedicine and tele-health care.

10. Mandate insurance coverage of screening and treatment of asymptomatic (subclinical) atherosclerosis.

In conclusion, to build the “Field of Dreams” for preventive cardiology and ultimately for the eradication of heart attacks, the government and health-care policy makers need to take the first step to build the ground.

HEART ATTACKS CAN BE ERADICATED

The heart attack epidemic inherited from the twentieth century (over 15million heart attacks every year), makes it difficult for most people to imagine a future in which heart attacks are no longer a threat. Nonetheless, the mission of eradicating heart attacks is no more challenging than the mission of landing humans on Mars. The vision for a heart attack-free future can become a reality in the twenty-first century and can result in a major increase in human life expectancy and socioeconomic development, if the medical community, including academia, industry, and health-care policymakers, shift their investment from the treatment of events that have already occurred to prevention of the first event. Figure 9 illustrates a likely path to arrest the worldwide epidemic of ACVD related mortality and morbidity, particularly heart attacks.

Heart-healthy life style assisted by innovative preventive technologies and personalized medicine will be able to shift the existing in-hospital expensive sick care to the future out-of-hospital inexpensive health care.

1. Era of Screening: Searching for and saving the vulnerable patient: as presented in the SHAPE Task Force report [7], the SHAPE initiative presents the best available strategy to advance the ongoing fight against ACVD, primarily heart attack and stroke [18].

2. Era of “PolyPill”: Mass prophylactic therapy of at-risk population using an effective, safe, and inexpensive cocktail of drugs: A future with universal prophylactic therapy for the prevention of ACVD, using a cocktail
of effective, safe, and inexpensive drugs (packaged compactly) to assure maximum compliance, is on the horizon. Although such a future is most desirable, there are major scientific and regulatory roadblocks that will require time and further investigations [16]. Pending resolution of these issues, the SHAPE strategy remains the best strategy.

3. Era of Vaccine: Primary prevention through immune modulation and vaccination strategies: Vaccination and immune modulation strategies for prevention, regression, and stabilization of atherosclerosis present a most exciting possibility. Atherosclerosis bears many similarities to chronic inflammatory/autoimmune diseases such as rheumatoid arthritis and Alzheimer’s disease. Compelling data from experimental models show that such diseases may be challenged by vaccination and immune modulation strategies. Will it be possible to attack ACVD with the same approach? Several studies have shown positive effects of immunization with antigenic LDL preparations. Such ground-breaking approaches may become the panacea for the world’s growing epidemic of heart disease [17].

CONCLUSION

Innovation in prevention will shape the future of cardiovascular health care. Heart attacks will be eradicated in the twenty-first century if the medical community, including academia, industry, and health-care policymakers, shift their investment from the treatment of events that have already occurred to prevention of the first event, i.e., “lock the barn door before the horse is stolen.”

REFERENCES

From Vulnerable Plaque to Vulnerable Patient

Morteza Naghavi and Erling Falk

On behalf of the vulnerable patient Consensus writing group*

CONTENTS

KEY POINTS
INTRODUCTION
UNDERLYING CAUSES OF SUDDEN, FATAL AND NONFATAL CARDIAC EVENTS
THE CHALLENGE OF TERMINOLOGY: CULPRIT PLAQUE VERSUS VULNERABLE PLAQUE
BEYOND THE ATHEROSCLEROTIC PLAQUE
DEFINITION OF A CARDIOVASCULAR VULNERABLE PATIENT
DIAGNOSIS OF VULNERABLE PLAQUE/ARTERY
FUNCTIONAL VersUS STRUCTURAL ASSESSMENT
PAN-ARTERIAL APPROACH
VULNERABLE (THROMBOGENIC) BLOOD
COAGULATION/ANTICOAGULATION SYSTEM
VULNERABLE MYOCARDIUM
RISK ASSESSMENT FOR VULNERABLE PATIENTS
NEW RISK ASSESSMENT STRATEGIES
REFERENCES

ABSTRACT

Atherosclerotic cardiovascular disease results in millions of sudden deaths annually, and coronary artery disease accounts for the majority of this toll. Despite major advances in the treatment of coronary artery disease, a large number of victims of the disease who are apparently healthy die suddenly without prior symptoms. Available screening and diagnostic methods are insufficient to identify the victims before the event occurs. The recognition of the role of the vulnerable plaque has opened new avenues in the field of cardiovascular medicine. This consensus document concludes the following. (1) Rupture-prone plaques are not the only vulnerable plaques. All types of atherosclerotic plaques with high likelihood of thrombotic complications and rapid progression should be considered as vulnerable plaques. We propose a classification for clinical as well as pathological evaluation of vulnerable plaques. (2) Vulnerable plaques are not the only culprit factors for the development of acute coronary syndromes, myocardial infarction,