

Review Article

The Effect of Antihypertensive Drugs on Endothelial Function as Assessed by Flow-Mediated Vasodilation in Hypertensive Patients

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Endothelial dysfunction is found in hypertensive patients and may serve as a prognostic marker of future cardiovascular events. Endothelial function can be assessed noninvasively by flow-mediated vasodilation (FMD). The goal of this paper is to summarize comprehensively the clinical trials that investigated the effects of antihypertensive drugs on endothelial function assessed by FMD in hypertensive patients. A PubMed-based search found 38 clinical trial papers published from January 1999 to June 2011. Significant improvement of FMD after antihypertensive treatment was shown in 43 of 71 interventions (among 38 clinical trial papers). Angiotensin II receptor blockers and angiotensin converting enzyme inhibitors appeared to improve FMD more than other drug types. Antihypertensive treatment can improve endothelial dysfunction when assessed by FMD, although there are conflicting data that require further research.

1. Introduction

Atherosclerotic risk factors such as hypertension (HTN), diabetes mellitus, dyslipidemia, obesity, and smoking cause endothelial dysfunction [1–5]. Endothelial dysfunction occurs in the early stages of atherosclerosis and is involved in disease progression as well as the morbid cardiovascular events that often occur in advanced stages of the diseases [1–5]. The endothelium is involved in the control of the coagulation/fibrinolytic system, platelet aggregation, adhesion of leukocytes, and smooth muscle cell proliferation and is important in the maintenance of vascular tone [1, 3]. The response-to-injury hypothesis, proposed by Russell Ross [6], states that atherosclerosis is due to an inflammatory reaction in response to endothelial injury or dysfunction and is supported by numerous basic and clinical investigations [1, 3].

The evaluation of endothelial function is available as a predictor of cardiovascular events and as a surrogate marker for early atherosclerosis [1–3, 7, 8]. There are several methods to evaluate endothelial function that include an invasive method using endothelium-dependent vasodilators

injected into a coronary or peripheral artery [7], and flow-mediated vasodilation (FMD), a noninvasive method based on endothelium-dependent arterial vasodilation [9, 10]. FMD was first reported in 1992 by Celermajer et al., as an innovative method of detecting endothelial dysfunction [10]. The sudden release of an artery after transient occlusion causes an increase in shear stress on the vessel wall due to hyperemia and this stimulates endothelial cells to release various physiologically active substances. Nitric oxide (NO) is one of the main substances released by the endothelium and causes relaxation of vascular smooth muscle with a subsequent increase in vascular diameter [1]. FMD is measured from the expansion rate of arterial diameter during the postischemic hyperemia response. Since guidelines for the measurement of FMD have been established [9] and the measuring equipment has been improved, FMD is gaining acceptance as a simple, safe, and valuable method to evaluate endothelial function in clinical practice.

HTN is prevalent worldwide and one of the most important risk factors for atherosclerotic disease [11, 12]. The relationship between FMD and blood pressure has been reported in a general population [13, 14]. FMD was

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Antihypertensive Treatment and Endothelial Vasodilatory Function Bengt Von Zur Muhlen, 2001 **Vascular Endothelium in Human Physiology and Pathophysiology** Patrick J Vallance, David J. Webb, 2003-09-02 Endothelial dysfunction is now regarded as an early marker of vascular disease and therefore an important target for therapeutic intervention and discovery of novel treatments Ideal for both basic and clinical scientists whether in industry or academia and physicians **Vascular Endothelium in Human Physiology and Pathophysiology** provides an up to date review of the vascular functions of the endothelium and its role in key areas of cardiovascular disease It focuses on evidence from studies in humans **Endothelial Function in Hypertension** David Webb, Patrick Vallance, 2012-12-06 The vascular endothelium has become an increasing focus of research over the last 15 years Nitric oxide and endothelin appear to have important and opposing actions on vascular tone smooth muscle proliferation and platelet monocyte activation and endothelial dysfunction affecting the L arginine nitric oxide and endothelin systems both appear to be crucial to atherogenesis and to the pathophysiology of many forms of cardiovascular disease Additionally a number of new drugs of major clinical interest are now emerging that act favourably to modulate endothelial function and alter the outcome in these conditions Here a synthesis of the current understanding of endothelial dysfunction in hypertension and related disorders and future therapeutic prospects has been drawn together by a series of internationally recognised leaders in the field Manual of Hypertension of the European Society of Hypertension Giuseppe Mancia, Guido Grassi, 2014-06-22 Despite recent advances in healthcare hypertension is a leading cause of death and remains a disease burden worldwide Now in its second edition the Manual of Hypertension of the European Society of Hypertension reflects emerging concepts that have the potential to impact diagnostic and therapeutic approaches to this condition Updating all mater **Endothelial Dysfunctions in Vascular Disease** Raffaele De Caterina, Peter Libby, 2008-04-15 Bridging the gap between the laboratory and the bedside this timely volume illuminates the connection between endothelial dysfunction and vascular disease This comprehensive survey of atherosclerotic disease begins with biology incorporating the latest breakthroughs in the field then elucidates risk factors and diagnostic tools and markers A major section on endothelium directed prevention and therapy shows you how to apply cutting edge research to clinical care Under the careful editorial guidance of Drs De Caterina and Libby the highly regarded contributors address endothelial activation and the initiation of atherosclerosis mechanisms of plaque progression and complications the role of LDL in the origin and progression of atherosclerosis advanced glycation endproducts and the accelerated atherosclerosis in diabetes oxidative stress and vascular disease soluble adhesion molecules as markers of vascular disease hormone replacement therapy and cardiovascular risk anti oxidants and endothelial protection and more The first book dedicated to the central role of endothelial dysfunction in vascular disease this concise volume gathers all the latest information on the subject into one convenient and cohesive text Make sure your patients are benefiting from current

knowledge by keeping a copy of Endothelial Dysfunctions in Vascular Disease close at hand for frequent consultation

Introduction Every book has a history this one not excepted having emerged from intersections in professional lives of the Editors This book bears the fruits of a collaboration between the pupil RDC and the mentor PL During an extended sabbatical of the pupil in Boston in 1994 we probed together the concept that endothelial dysfunction served as a common denominator of vascular disease with the balance between inflammation and its inhibition as a fulcrum of the regulation of the behavior of endothelial cells As practicing cardiologists in our clinical lives we sought to link to endothelial function the mechanisms of action of risk factors and of pharmacologic agents used to treat and prevent vascular disease The pupil therefore authored a few reviews on the mechanism of action of risk factors and included them in a small book published in Italian for which the mentor wrote a preface The book was greeted with favor from the Italian cardiological community and provided the nidus for the present more ambitious endeavor which includes updated reviews on the pathogenesis of vascular disease and on the most novel aspects of vascular biology This enterprise was enabled by the contributions of many of our former or present collaborators and colleagues without whose enthusiasm and engagement this work could never have seen light We largely underestimated the devotion necessary on our own side at the beginning but it ultimately yielded a product that we feel achieves our original goals We are aware that we confront a continuously evolving topic where frequent updates would be desirable if not necessary Yet we believe in the value of books such as the current one that attempt to organize in a snapshot of time the vast amount of literature available in a coherent and comprehensive scheme We are aware of existing gaps of emerging material not paid its due and of the rapid evolution of some of the concepts highlighted within The links between the laboratory and the clinic have never afforded more opportunity for new understanding and advances in diagnosis and treatment than today We hope that our colleagues vascular biologists cardiologists internists and other physicians alike will find this compendium a useful guide to this most exciting time in vascular biology and medicine Raffaele De Caterina and Peter Libby

Antioxidants and Cardiovascular Disease J.C. Tardif, Martial G. Bourassa, 2012-12-06 Generation of oxidants or reactive oxygen species is a natural process of human biology Mitochondrial respiration phagocytic activity and cyclooxygenase activation are all essential processes of life which also generate oxidative species In humans chronic oxidative stress often coupled with deficiency of antioxidant defenses is associated with the aging process and can lead to the development of disorders such as cancer and arterial disease Major cardiovascular conditions in which oxidative damage has been strongly implicated include atherosclerosis myocardial ischemia and reperfusion coronary restenosis and congestive heart failure Compelling evidence points to oxidative stress as an important trigger in the complex chain of events leading to atherosclerosis The expression of chemotactic factors and adhesion molecules is modified by oxidative stress Exposure to superoxide ions activates the NF kappa B regulatory complex and triggers the transcription of several atherosclerosis related genes These events lead to the accumulation of macrophages in the arterial wall Macrophages avidly incorporate oxidized

low density lipoproteins LDL to form foam cells The activity of matrix metalloproteinases is also regulated by oxidative stress This activity appears to be closely coupled with smooth muscle cell activation and migration Matrix metalloproteinases have also been implicated in the pathophysiology of plaque rupture Antioxidant supplementation including vitamin E decreases susceptibility of LDL to oxidation and retards the progression of atherosclerosis in animal models **The Vascular**

Endothelium II Salvador Moncada, Annie Higgs, 2006-10-14 This wide ranging work provides a complete representation of the present state of knowledge of the vascular endothelium The volume comprises 20 chapters by experts who have made significant contributions to research in the vascular endothelium The text discusses the structure development and function of the normal vascular endothelium considers conditions that lead to the disruption of vascular physiology and provides a comprehensive description of pathologies and their treatment *Antioxidants and Cardiovascular Disease* Martial G. Bourassa, Jean-Claude Tardif (M.D.), 2006 Chronic oxidative stress is associated with the aging process and often leads to the development of disorders such as cancer and arterial disease Cardiovascular conditions in which oxidation damage has been strongly implicated include atherosclerosis myocardial ischemia and reperfusion coronary restenosis diabetes mellitus and congestive heart failure *Antioxidants and Cardiovascular Disease Second Edition* covers three major topics 1 the first seven chapters review the oxidative modification hypothesis and its close relationship to lipid metabolism and to the pathogenesis of atherosclerosis 2 the next four chapters describe the different compounds nutrients and supplements with antioxidant properties and their mechanisms of action 3 and finally the last ten chapters discuss the potential benefits of antioxidants in overall cardiovascular prevention including hypertension diabetes mellitus dyslipidemias and in the treatment and prevention of specific conditions such as chronic coronary artery disease restenosis after percutaneous coronary intervention and chronic heart failure *Antioxidants and Cardiovascular Disease Second Edition* is written by recognized experts in the fields of atherosclerosis heart failure and antioxidants It should be of interest to medical students and fellows researchers and practicing physicians There has been rapid progress in our knowledge in this field during the last two to three years Thus the current reedition appears timely For instance this second edition captures several recently reported and published clinical trials as well as new information on diabetic and hypertensive cardiovascular disease **Hypertension: A Companion to**

Braunwald's Heart Disease E-Book Henry R. Black, William Elliott, 2012-08-01 Effectively manage the chronic problems of your hypertensive patients with the practical clinical tools inside *Hypertension 2nd Edition A Companion to Braunwald's Heart Disease* This respected cardiology reference covers everything you need to know from epidemiology and pathophysiology through diagnosis risk stratification treatment outcome studies concomitant diseases special populations and special situations and future treatments Confidently meet the needs of special populations with chronic hypertensive disease as well as hypertension and concomitant disease Learn new methods of aggressive patient management and disease prevention to help ensure minimal risk of further cardiovascular problems Benefit from the authors Clinical Pearls to reduce

complications of hypertension Use new combination drug therapies and other forms of treatment to their greatest advantage in the management of chronic complications of hypertension Successfully employ behavior management as a vital part of the treatment plan for hypertensives and pre hypertensives

Diabetes, hypertension and cardiovascular diseases, volume II Soo-Kyoung Choi, María Galán, Modar Kassan, 2023-02-10 Atherosclerosis and Oxidant Stress: A New Perspective Jordan L Holtzman, 2007-09-26 Vascular injury is initiated by oxidant injury to the vessel wall This volume is organized around the role of oxidant damage in this disease process and provides a collection of the most recent studies representing various disciplines that can serve as the basis for further improvements in our understanding and control of cardiovascular and cerebral vascular disease

TRP Ion Channel Function in Sensory Transduction and Cellular Signaling Cascades Wolfgang B. Liedtke, MD, PH.D., 2006-09-29 Since the first TRP ion channel was discovered in *Drosophila melanogaster* in 1989 the progress made in this area of signaling research has yielded findings that offer the potential to dramatically impact human health and wellness Involved in gateway activity for all five of our senses TRP channels have been shown to respond to a wide range of stimuli

Cardio-Protection and Heart Repair: New Drugs, Targets and Approaches Benzhi Cai, Hua Zhu, Naufal Zagidullin, 2022-01-19 *Thrombosis and Hemorrhage* Joseph Loscalzo, Andrew I. Schafer, 2003 Now in its Third Edition this authoritative text continues to provide a comprehensive and systematic review of the biology pathobiology and clinical disorders of the hemostatic system Its unique organization of the basic sciences coupled with clinical sections yields a user friendly integrated text and a reference tool that meets the needs of diverse investigators and clinicians of contemporary medicine for understanding the hemostatic system New chapter topics covered in this edition include angiogenesis and vasculogenesis hemorrhagic complications of antithrombotic therapy interactions of coagulation and fibrinolytic proteins with the vessel wall and less common thrombotic disorders

Atherothrombosis and Coronary Artery Disease Valentin Fuster, Eric J. Topol, Elizabeth G. Nabel, 2005 Written by the world's foremost authorities this volume provides comprehensive coverage of current approaches to the prevention diagnosis and management of atherothrombosis and its coronary and noncoronary complications This edition has been thoroughly updated sharply focused on clinical information and trimmed to one manageable volume Coverage begins with a review of risk factors and prevention emphasizing lipid abnormalities hypertension smoking diabetes and obesity Subsequent sections examine the pathogenesis of atherosclerosis markers and imaging acute coronary syndromes chronic stable angina and noncoronary atherothrombosis Clinical presentations medical management and the latest interventional strategies are included

Women's Health and Menopause Rodolfo Paoletti, P.G. Crosignani, P. Kenemans, N.K. Wenger, Ann S. Jackson, 2007-07-11 The population structure in the world is rapidly changing to the extent that in 75 years we will face a tripling of the elderly population Although women are favored in terms of life expectancy they also live with a longer period of disability approximately twice that of aging men as well as with the enemies of all the elderly cardiovascular disease cancer and dementia Menopause is the

endocrine event that overlaps with aging potentially worsening both the quality of life and the risks of disease in women While the effect of hormone replacement therapy HRT on menopausal symptoms is generally viewed as rapid and consistent and is thereby accepted by the scientific community its relationship to the other aforementioned chronic conditions associated with menopause is considered variable and controversial In analyzing these complex issues this volume yields new and significant insights into both the study of menopause related disorders and their treatment by illustrating the most recent information on mechanisms of actions of new estrogen receptors and on the use of sophisticated techniques of statistical analysis for population based studies Principles and Practice of Endocrinology and Metabolism Kenneth L. Becker,2001 Established as the foremost text in the field Principles and Practice of Endocrinology and Metabolism is now in its thoroughly revised updated Third Edition This practical clinically relevant and comprehensive text covers the entire field of endocrinology and metabolism including the diffuse endocrine system morphology and physiology diagnosis and treatment of endocrine diseases endocrinology of the female hormones and cancer and much more The Third Edition contains new chapters reflecting the latest advances and features expanded coverage of genetics and the endocrinology of sepsis More than 1 400 illustrations complement the text A drug formulary appears at the back of the book *Hypertension* Henry R. Black,William Elliott,2006-12-28 Clinical hypertension is one of the most serious long term problems associated with heart disease This companion to Braunwald s Heart Disease focuses in depth on this key area of cardiovascular medicine Complete with practical clinical tools for management it helps you manage the chronic problems of your hypertensive patients It covers everything from epidemiology and pathophysiology through diagnosis risk stratification treatment outcome studies concomitant diseases special populations and special situations and future treatments Addresses management of all special populations with chronic hypertensive disease Includes Clinical Pearls for reducing complications of hypertension Discusses hypertension and concomitant disease Provides information on the practical management of hypertension and its role in complex diseases Emphasizes prevention of hypertensive diseases Covers behavior management as an integral part of treatment plan for hypertensives and pre hypertensives Assesses drugs and other forms of treatment Presents current clinical guidelines for the U S Canada and Europe Encourages aggressive patient management to ensure minimal risk of further cardiovascular problems *Hypertension and the Heart* Alberto Zanchetti,Richard B. Devereux,Lennart Hansson,Sergio Gorini,2012-12-06 Proceedings of the International Conference held as Part of the Menarini Series on Cardiovascular Diseases in Berlin Germany February 27 28 1998 **Cumulated Index Medicus** ,1996

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