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Original research

Long-term survival benefit of ramipril in patients with acute myocardial infarction complicated by heart failure

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ABSTRACT

Aims ACE inhibition reduces mortality and morbidity in patients with heart failure after acute myocardial infarction (AMI). However, there are limited randomised data about the long-term survival benefits of ACE inhibition in this population.

Methods In 1993, the Acute Infarction Ramipril Efficacy (AIRE) study randomly allocated patients with AMI and clinical heart failure to ramipril or placebo. The duration of masked trial therapy in the UK cohort (603 patients, mean age=64.7 years, 455 male patients) was 12.4 and 13.4 months for ramipril (n=302) and placebo (n=301), respectively. We estimated life expectancy and extensions of life (difference in median survival times) according to duration of follow-up (range 0–29.6 years).

Results By 9 April 2019, death from all causes occurred in 266 (88.4%) patients in placebo arm and 275 (91.1%) patients in ramipril arm. The extension of life between ramipril and placebo groups was 14.5 months (95% CI 13.2 to 15.8). Ramipril increased life expectancy more for patients with than without diabetes (life expectancy difference 32.1 vs 5.0 months), previous AMI (20.1 vs 4.9 months), previous heart failure (19.5 vs 4.9 months), hypertension (16.6 vs 8.3 months), angina (16.2 vs 5.0 months) and age >65 years (11.3 vs 5.7 months). Given potential treatment switching, the true absolute treatment effect could be underestimated by 28%.

Conclusion For patients with clinically defined heart failure following AMI, ramipril results in a sustained survival benefit, and is associated with an extension of life of up to 14.5 months for, on average, 13 months treatment duration.

INTRODUCTION

Survival following acute myocardial infarction (AMI) remains a key objective for healthcare professionals and governments throughout the globe. Despite major advances in the emergency treatment and secondary prevention of AMI, a substantial proportion of patients with AMI develop heart failure,¹ which in turn is associated with high morbidity, mortality and healthcare expenditure.^{2–4}

Moreover, therapeutic inhibition of ACE has become an established strategy in the care of patients with AMI and heart failure.⁵ ACE inhibition reduces death and disease in patients with left ventricular systolic dysfunction, and coronary artery disease.^{6–8} In the Acute Infarction Ramipril

Efficacy (AIRE) study, ACE inhibition at an average follow-up time of 15 months after randomisation significantly reduced all-cause mortality, and continued to confer a survival benefit at 3 years following study closure in the AIRE Extension (AIREX) study.^{9–12} Further placebo-controlled survival studies testing the efficacy of ACE inhibition in patients with AMI and clinical heart failure are unlikely because withholding a treatment of accepted clinical value would be unethical. Therefore, in the AIRE survival (AIRE-S) study, we aimed to assess the long-term (29.6 years after randomisation) magnitude of impact on length of survival observed after treatment with ramipril (target dose 5 mg twice daily) when compared with placebo.

METHODS

Patients and design

The rationale, design, organisation, outcome definitions and results of the AIRE study have been published previously.^{10–12} This was an independent, multinational, multicentre, double-blind, randomised, placebo-controlled, parallel-group investigation into the potential benefits from treatment with the lipophilic ACE inhibitor ramipril (target dose 10 mg/day) following AMI complicated by clinical evidence of heart failure. When the trial was conducted, in 1993, all patients had an ECG and cardiac enzyme confirmation of AMI, and also evidence of transient or persisting heart failure as judged by the attending physician (chest X-ray evidence of left ventricular failure, or auscultatory evidence of pulmonary oedema, or a third heart sound in the presence of persistent tachycardia), usually sufficient to justify diuretic or vasodilator therapy. Patients were excluded if they had evidence of clinical instability, contraindications to the use of ACE inhibitor therapy, heart failure of primary valvular or congenital origin or overt heart failure deemed to require treatment with an open-label ACE inhibitor. After applying these entry criteria to consecutive patients admitted to the UK centres (30 centres), 44% of patients approached declined to give their consent to take part in the study. All 603 of the remaining patients were then randomised by telephone to receive masked treatment with either ramipril (titrated over 4 days to 5 mg twice daily) or a matching placebo. Treatment was started between 2 and 9 days after the onset of AMI. Patients initially received either 1.25 or 2.5 mg ramipril or

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Long-Term Management of Patients After Myocardial Infarction C. Tissa Kappagoda,P. V. Greenwood,1987-11-01

Coronary Care Manual Peter L. Thompson,2010-12-03 The Coronary Care Manual has been designed as a practical manual for the management of the acute coronary patient and aims to achieve a balance between the large and rapidly changing evidence base and practical application in the CCU ICU ED and ambulance The book has been written by a group of Australian and international experts for medical nursing and paramedic staff working in these areas This edition covers a broad range of coronary care medicine in enough detail to eliminate the need to refer to a larger reference book providing a portable companion for a night on call Completely redesigned with new artwork the manual is organized to suit academics and practitioners alike covers a broad range of coronary care medicine provides specific advice on the management of common clinical problems eliminates the need to refer to a larger reference book features a consistent style and focus with standardised artwork for figures is now also available as an eBook A code inside the Coronary Care Manual enables a full text download allowing you to browse and search electronically make notes and bookmarks in the electronic files and highlight material

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Cumulated Index Medicus, 1994 *Drugs for the Heart E-Book* Lionel H. Opie, Bernard J. Gersh, 2011-12-01 The new edition of this market leading cardiac drug resource equips you with the latest advances in cardiovascular pharmacology one of the most rapidly changing areas of medicine It not only offers in depth information on all of the drug classes used to treat heart disease but also covers new drug classes drug use for single and multiple problem management and more Dynamic full color drawings illustrate key pharmacological and physiological actions and a user friendly organization directs you to the information you need An increased emphasis on the practical use of drugs saves you valuable time in researching relevant information Features the practice proven experience of two well known editors who represent the best possible combination of clinical and research expertise in cardiovascular therapeutics Offers easy to access useful information on when to use each drug and for what conditions in a chapter entitled Which Drug for Which Disease Discusses the management of single diseases and multiple comorbidities Summarizes each drug class at the end of chapters to expedite reference Incorporates all new drugs preparations and clinical trial data in each chapter equipping you to make the most up to date informed clinical decisions Offers expanded coverage of comorbid diseases through new chapters on metabolic syndrome hyperglycemia and diabetes Features an increased emphasis on the practical use of drugs through highlighted sections and key illustrations saving you time in searching for relevant information Presents the work of several new contributors who represent a broad international perspective to equip you with a global view of cardiovascular pharmacology **Index Medicus**, 2001

Geriatric Medicine Christine K. Cassel, Rosanne Leipzig, Harvey Jay Cohen, Eric B. Larson, Diane E. Meier, 2006-05-29

Since the publication of the third edition of Geriatric Medicine extraordinary advances have occurred in the science of aging and the potential for biomedical research to give us answers to many if not most of the age related disorders that threaten the quality of life in older years At the most basic level the successful mapping of the human genome was declared complete in the fall of 2000 Understanding the map of the human genome is as important as understanding the map of genomes of important laboratory species ranging from the microscopic worms and fruit flies used in most classic genetic studies to rodents such as laboratory mice and eventually to primates on which much of the research on the aging human brain is done The genetic maps of all of these species including our own does not answer clinical questions but it does open the door to dramatic rapid and efficient answers to questions about the genetic polymorphisms related to diseases in humans The telomerase story also unfolded since the third edition Telomerase is an enzyme responsible for maintaining the telomeres the redundant DNA portions at the end of chromosomes whose shortening seems to be linked directly to cell senescence apoptosis and the control over cell death which at the level of the individual cell seems to be linked to the decline of organ function and eventually aging and death within the organism Reichel's Care of the Elderly Christine Arenson, Jan

Busby-Whitehead, Kenneth Brummel-Smith, James G. O'Brien, Mary H. Palmer, William Reichel, 2009-02-09 The sixth edition remains the pioneering text for the practising physician confronted with the unique problems of an increasingly elderly population Dr William Reichel's formative text is designed as a practical and useful guide for health specialists from medical students to practicing physicians This book is not a collection of subspecialty chapters but rather emphasizes the clinical management of the geriatric patient with simple to complex problems The editors have reviewed every chapter and have included the most up to date advances in the care of the elderly New chapters include hormonal therapy in post menopausal women drug therapy for Alzheimer's sufferers alternative medicine the chronic understaffing of nursing homes management of delirium and ethical issues Comprehensive and written for any clinicians caring for older patients including family physicians general internists nurse practitioners geriatricians and other specialists this esteemed text provides practical and trusted advice Hemostasis and Thrombosis Victor J. Marder, William C. Aird, Joel S. Bennett, Sam Schulman, Gilbert C.

White, II, 2012-12-27 Since publication of the First Edition in 1982 Hemostasis and Thrombosis has established itself as the pre eminent book in the field of coagulation disorders No other book is as inclusive in scope with coverage of the field from the standpoint of both basic scientists and clinicians This comprehensive resource details the essentials of bleeding and thrombotic disorders and the management of patients with these and related problems and delivers the most up to date information on normal biochemistry and function of platelets or endothelial cells as well as in depth discussions of the pharmacology of anticoagulant fibrinolytic and hemostatic drugs NEW to the Sixth Edition A new team of editors each a leader in his field assures you of fresh authoritative perspectives Full color throughout A companion website that offers full

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becoming increasingly difficult to remain abreast of these advances in each individual modality and thus it is no longer practical to focus on one at a time In addition training guidelines are changing and multimodality training has become the norm Multimodality Imaging in Cardiovascular Medicine presents a clear and in depth review of the available technologies and evidence supporting their appropriate clinical applications Hundreds of outstanding images are included to support and augment the discussions from the leading experts in each modality For maximum clinical value rather than organize the content by imaging modality the book is organized by disease so that the reader can utilize the book in real time problem solving and decision making in daily clinical practice Features of Multimodality Imaging in Cardiovascular Medicine Include More than 350 multimodality imaging examples of cardiovascular pathophysiology Corresponding text places the images into context at the interface with patient care State of the art chapters contributed by the leading imaging experts *Sabiston Textbook of Surgery E-Book* Courtney M. Townsend Jr., R. Daniel Beauchamp, B. Mark Evers, Kenneth L. Mattox, 2015-05-26 LIC Sabiston Textbook of Surgery **Braunwald's Heart Disease E-Book** Robert O. Bonow, Douglas L. Mann, Douglas P. Zipes, Peter Libby, 2011-02-25 Braunwald's Heart Disease remains your indispensable source for definitive state of the art answers on every aspect of contemporary cardiology Edited by Drs Robert O Bonow Douglas L Mann Douglas P Zipes and Peter Libby this dynamic multimedia reference helps you apply the most recent knowledge in molecular biology and genetics imaging pharmacology interventional cardiology electrophysiology and much more Weekly updates online personally selected by Dr Braunwald continuously keep you current on the most important new developments affecting your practice Enhanced premium online content includes new dynamic cardiac imaging videos heart sound recordings and podcasts With sweeping updates throughout and contributions from a who's who of global cardiology Braunwald's is the cornerstone of effective practice Continuously access the most important new developments affecting your practice with weekly updates personally selected by Dr Braunwald including focused reviews hot off the press commentaries and late breaking clinical trials Practice with confidence and overcome your toughest challenges with advice from the top minds in cardiology today who synthesize the entire state of current knowledge and summarize all of the most recent ACC AHA practice guidelines Locate the answers you need fast thanks to a user friendly full color design with more than 1 200 color illustrations Search the complete contents online at www.expertconsult.com Stay on top of the latest advances in molecular imaging intravascular ultrasound cardiovascular regeneration and tissue engineering device therapy for advanced heart failure atrial fibrillation management structural heart disease Chagas heart disease ethics in cardiovascular medicine the design and conduct of clinical trials and many other timely topics Hone your clinical skills with new dynamic cardiac imaging videos heart sound recordings and podcasts at www.expertconsult.com **Acute Coronary Syndromes: A Companion to Braunwald's Heart Disease E-Book** Pierre Theroux, 2010-09-24 Acute Coronary Syndromes a Companion to Braunwald's Heart Disease covers the state of the art scientific and clinical information you need to rapidly evaluate and manage acute coronary syndromes Dr Pierre

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Stem Cell and Gene Therapy for Cardiovascular Disease Emerson c. Perin, Leslie W. Miller, Doris Taylor, James T. Willerson, 2015-08-21 Stem Cell and Gene Therapy for Cardiovascular Disease is a state of the art reference that combines in one place the breadth and depth of information available on the topic As stem cell and gene therapies are the most cutting edge therapies currently available for patients with heart failure each section of the book provides information on medical trials from contributors and specialists from around the world including not only what has been completed but also what is planned for future research and trials Cardiology researchers basic science clinicians fellows residents students and industry professionals will find this book an invaluable resource for further study on the topic Provides information on stem and gene therapy medical trials from contributors and specialists around the world including not only what has been completed but also what is planned for future research and trials Presents topics that can be applied to allogeneic cells mesenchymal cells gene therapy cardiomyocytes iPS cells MAPC s and organogenesis Covers the three areas with the greatest clinical trials to date chronic limb ischemia chronic angina and acute MI Covers the prevailing opinions on how to harness the body s natural repair mechanisms Ideal resource for cardiology researchers basic science clinicians fellows residents students and industry professionals *Coronary Care Medicine* E. Antman, J.D. Rutherford, 2012-12-06 Attention to reducing the major risk factors Contemporary coronary care involves a associated with the development of arterio multitude of measures efforts to prevent the sclerosis has been widespread and appears to acute event thrombolytic therapy to abort have lowered the incidence of coronary artery infarction pharmacological measures to delay disease Nevertheless acute myocardial and reduce ischemic cell death monitoring of infarction and related ischemic syndromes the hemodynamic consequences of myocardial represent

the most common causes of death as infarction treatment of acute pump failure use well as one of the principal reasons for of modern electrical devices as well as a large hospitalization in the industrialized world In number of new drugs to prevent and treat light of this care of the patient with acute cardiac arrhythmias and finally identification coronary disease remains a major medical prior to hospital discharge of patients who are at challenge high risk for recurrent infarction or sudden The approach to managing patients with death and the choice of the appropriate acute myocardial infarction can be said to have management approach evolved through three major phases For the This fine book provides comprehensive first half century after Herrick s landmark descriptions of these various aspects of paper describing this condition was published in contemporary coronary care It is accurate 1912 management consisted primarily of thorough and easily readable

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