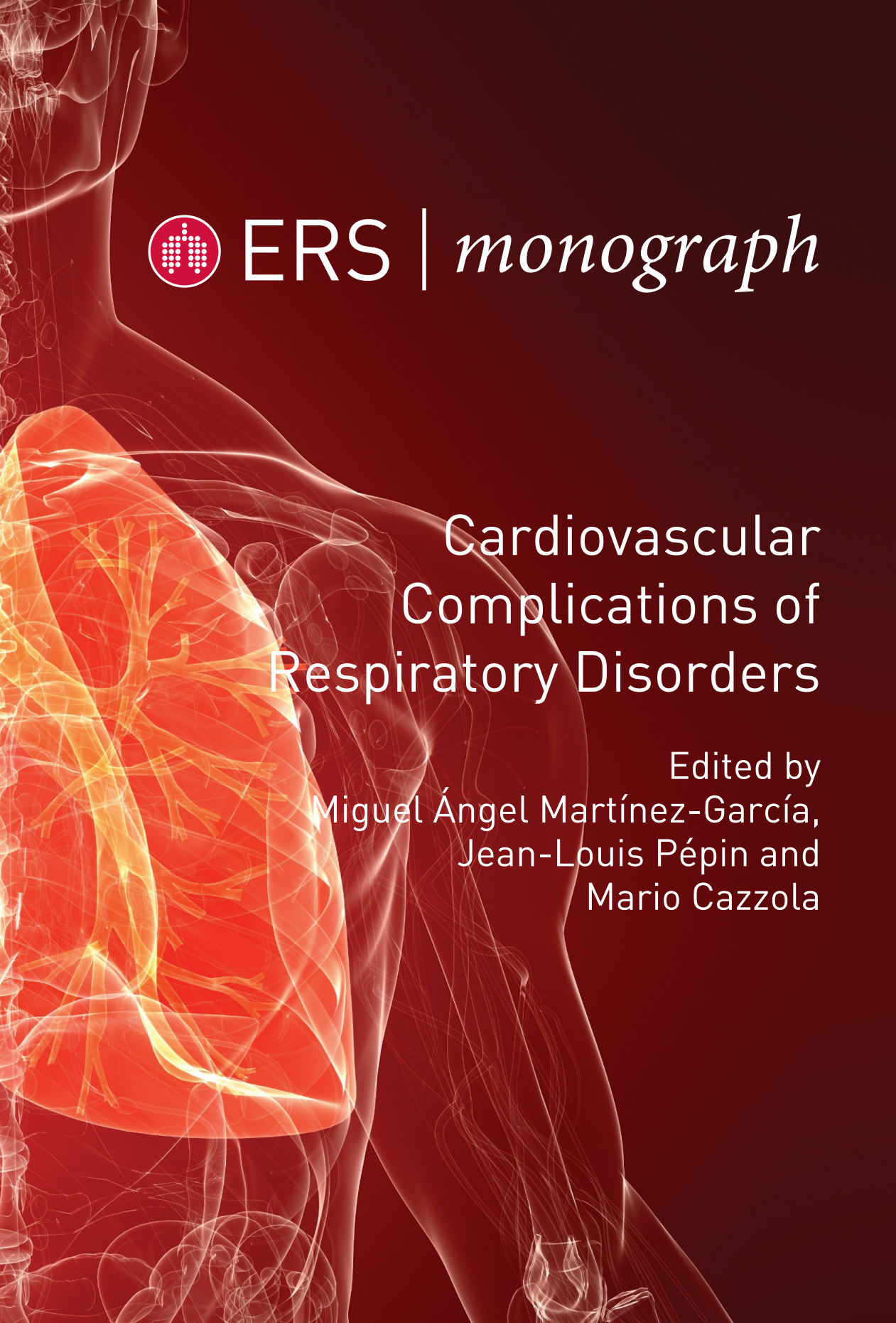

ERS | *monograph*

Cardiovascular Complications of Respiratory Disorders

Edited by
Miguel Ángel Martínez-García,
Jean-Louis Pépin and
Mario Cazzola

Cardiovascular Complications of Respiratory Disorders

Edited by
Miguel Ángel Martínez-García,
Jean-Louis Pépin and Mario Cazzola

Editor in Chief
John R. Hurst

This book is one in a series of *ERS Monographs*. Each individual issue provides a comprehensive overview of one specific clinical area of respiratory health, communicating information about the most advanced techniques and systems required for its investigation. It provides factual and useful scientific detail, drawing on specific case studies and looking into the diagnosis and management of individual patients. Previously published titles in this series are listed at the back of this *Monograph*.

ERS Monographs are available online at www.books.ersjournals.com and print copies are available from www.ersbookshop.com

Published by European Respiratory Society ©2020
June 2020
Print ISBN: 978-1-84984-118-4
Online ISBN: 978-1-84984-119-1
Print ISSN: 2312-508X
Online ISSN: 2312-5098
Typesetting by Nova Techset Private Limited

ERS | monograph

Contents

Cardiovascular Complications of Respiratory Disorders

Number 88
June 2020

ERS | *monograph*

Preface

John R. Hurst

CVD remains the most common cause of death in the world and people living with respiratory disease are at increased risk of cardiovascular events. Only by understanding the science that links both acute and chronic respiratory disease with cardiovascular events, such as myocardial infarction and stroke, and by using this knowledge to provide holistic care, can we ever hope to achieve the best outcome for our patients. It is therefore a pleasure to introduce and recommend to you this latest *ERS Monograph*, which focuses on the cardiovascular implications of respiratory disease, including the cardiovascular effects of drugs that we commonly use in respiratory medicine.

One of the privileges of acting as Chief Editor of the *Monograph*, and serving on the Editorial Board, is selecting topics for future editions. We do this by considering the latest developments in respiratory medicine, reader surveys and analysing the use of previous editions. But this edition was different: the Guest Editors, Miguel Ángel Martínez-García, Jean-Louis Pépin and Mario Cazzola, came to the Editorial Board with a proposal and I congratulate and thank them for having the vision to develop the idea, and the skill and determination to deliver this excellent, state-of-the-art collection of review articles. They have assembled an impressive and authoritative collection of chapters. I would like to take this opportunity to also thank all the contributors.

Whether you are a respiratory scientist or clinician, specialist or generalist, there is a topic and information for you here that is interesting and important. Read on!

Disclosures: J.R. Hurst reports receiving grants, personal fees and non-financial support from pharmaceutical companies that make medicines to treat respiratory disease. This includes reimbursement for educational activities and advisory work, and support to attend meetings.

 Print ISBN: 978-1-84984-118-4. Online ISBN: 978-1-84984-119-1. Print ISSN: 2312-508X. Online ISSN: 2312-5098.

ERS | *monograph*

Guest Editors

Miguel Ángel Martínez-García

Miguel Ángel Martínez-García is Section Head, Research Coordinator and Sleep Disordered Breathing Head of the Pulmonary Disorder Division of the University and Polytechnic La Fe Hospital in Valencia, Spain. His research mainly focuses on OSA and airway diseases, particularly bronchiectasis and COPD.

Miguel Ángel is the author/co-author of six national/international guidelines or task forces on sleep apnoea, bronchiectasis and COPD, and has had >200 peer reviewed scientific papers published. He has edited 10 books on respiratory diseases, and has received >40 grants and 12 scientific awards from national and international societies, including best reviewer of the *European Respiratory Journal* (*ERJ*) in 2014. His H-index is 36.

Miguel Ángel has been a speaker at >200 invited lectures at national and international meetings.

Miguel Ángel is currently a fellow of the European Respiratory Society (ERS), an Associate Editor of the *ERJ* and is a member of ERS' sleep working group educational council. He is also a member of the bronchiectasias–airway disease working group of EMBARC (European Multicentre Bronchiectasis Audit and Research Collaboration). He has a Masters in airways disease, bronchiectasis and hospital management.

Miguel Ángel was previous a member of the Scientific Committee of and is currently a member of the International Committee of SEPAR (Spanish Society of Pneumology and Thoracic Surgery). He is Director of the Bronchiectasis Scientific Program Project (PII) and Chair of the Spanish Bronchiectasis Registry (RIBRON) of SEPAR.

 Print ISBN: 978-1-84984-118-4. Online ISBN: 978-1-84984-119-1. Print ISSN: 2312-508X. Online ISSN: 2312-5098.

 https://doi.org/10.1183/2312508X.10005320

Jean-Louis Pépin

Jean-Louis Pépin is Professor of Clinical Physiology at the University Grenoble-Alpes (UGA) (Grenoble, France). He is Head of the Clinic of Physiology, Sleep and Exercise at Grenoble University Hospital (CHUGA) (Grenoble, France), Director of the HP2 Laboratory (INSERM U1042, UGA; Hypoxia Pathophysiology), and vice-Dean of the Faculty of Medicine in charge of research and Scientific Director of clinical research at CHUGA. Jean-Louis is also the director of the UGA Chair of Excellence in e-health and integrated care and the Artificial intelligence Chair "Trajectories Medicine" (2018–2021).

Jean-Louis graduated as: MD in 1987 at the University of Montpellier (Montpellier, France); MSc in 1990, in biophysiology at the University Claude Bernard, Lyon, France; and PhD in 1998, in cardiovascular adaptations induced by chronic hypoxia, at the University Joseph Fourier, Grenoble. In 1999, he was Visiting Professor at the Laboratory of Pulmonary Physiology of Harvard University (Boston, MA, USA). He achieved European certification in sleep medicine in 2013.

Jean-Louis' interests include clinical and translational research on the cardiovascular consequences of chronic and intermittent hypoxia, sleep apnoea, COPD and chronic respiratory failure.

Jean-Louis runs the French National Prospective Registry of Sleep Apnea (RESAS), which has >120 000 subjects, and is involved in the European Sleep Apnea Database (ESADA). He has participated in several European and US thoracic society task forces, and is the former President of the French Sleep Research and Medicine Society. He has experience in innovation (he has >10 patents), in clinical trials and in industrial partnerships. He was the principle investigator of OPTISAS, a national telemedicine trial on sleep apnoea, and on LIFE, a transdisciplinary research program involving 70 researchers on evidence-based societal and environmental control of chronic diseases, funded by UGA-IDEX. He has been funded by EIT-Health for several European Union projects and is ranked third highest expert worldwide in the field of sleep apnea by Expertscape.

Jean-Louis is an Associate Editor of *Thorax*, is author/co-author of >450 scientific publications and has an H-index of 58.

Mario Cazzola

Mario Cazzola is an Honorary Professor of Respiratory Medicine at the University of Rome "Tor Vergata" (Rome, Italy) and at the Sackler Institute of Pulmonary Pharmacology, GKT School of Biomedical Sciences (London, UK).

Mario's research mainly focuses on the pharmacology of airway diseases, particularly the use of bronchodilators. According to Expertscape (February 2020), he is the top-rated expert in COPD and in bronchodilator agents in the world.

Mario is Chairman of the Southern Europe Chapter of Interasma and Chairman of the Med COPD Forum. He was previously: Chairman of the Airway Pharmacology and Treatment Group of the European Respiratory Society (ERS); Secretary of the Inflammatory Airway Diseases and Clinical Allergy Assembly of ERS; ERS Postgraduate Courses Director; an Internal Auditor at ERS; a member of the Steering Committee of the Airway Disorders Network and a Governor of the Italian Chapter of the American College of Chest Physicians. Mario was Co-Chair of the ERS/American Thoracic Society (ATS) Task Force "Outcomes for COPD pharmacological trials: from lung function to biomarkers". He is a Fellow of ERS and in 2015, received a Lifetime Achievement Award from the same society. He has acted as referee/assessor for different universities and agencies worldwide.

Mario founded *Therapeutic Advances in Respiratory Diseases* and served as its first Editor-in-Chief. He has also held the position of Editor-in-Chief of *Pulmonary Pharmacology and Therapeutics*, and *COPD Research and Practice*. He serves as an Associate Editor for *Respiratory Medicine*, *Respiratory Research*, *Current Research in Pharmacology and Drug Discovery*, *Clinical Investigation* and *The Open Respiratory Medicine Journal*. He is the author/co-author of almost 670 scientific papers. His H-index is 62.

https://doi.org/10.1183/2312508X.10005320

ERS | monograph

Introduction

Miguel Ángel Martínez-García[1], Jean-Louis Pépin[2] and Mario Cazzola[3]

@ERSpublications
Cardiovascular and respiratory diseases are two of the leading causes of all-cause mortality. Both are closely related. Knowing the relationship between the two groups of diseases is key to the management of the patient. https://bit.ly/3efOiN3

CVD and respiratory disease are two of the main causes of morbidity, mortality and health costs all over the world. The main organs affected by these diseases – the heart and lungs – are closely related in both physiological and pathological terms. Many CVDs, or their treatment, can affect the respiratory system, and the vast majority of lung diseases can involve or be associated with diseases of the cardiovascular system.

This close relationship probably reflects two fundamental circumstances: on the one hand, the high prevalence of these groups of diseases can mean that a single patient can suffer from both simultaneously, with one acting as a comorbidity of the other. This situation will become increasingly common, due to human beings' progressively greater longevity and the subsequent chronification of many diseases. On the other hand, both types of diseases share many of the same pathophysiological pathways and support mechanisms, as demonstrated in both murine models and human studies.

A knowledge of the potential cardiovascular implications and complications inherent in the most prevalent lung diseases, and their treatment, may be crucial for clinicians as they could have therapeutic implications for a respiratory disease and influence its prognosis.

Several studies have investigated the greater cardiovascular risk associated with lung diseases with a high inflammatory burden, such as COPD, asthma, and both acute and chronic respiratory infections. This situation may occur because such diseases share, or are capable of activating, some of the intermediate pathophysiological mechanisms in cardiovascular damage.

Some respiratory diseases, can, in the advanced stages of their evolution, affect cardiac function as a result of changes in vascular resistance or in the structure of the vessels. This is the case in pulmonary thromboembolism, some interstitial diseases and hypoventilation syndromes.

[1]Pneumology Dept, University and Politechnic La Fe Hospital, Valencia, Spain. [2]Grenoble University Hospital Center, Grenoble, France. [3]Unit of Respiratory Medicine, Dept of Experimental Medicine, University of Rome "Tor Vergata", Rome, Italy.

Correspondence: Miguel Ángel Martínez-García, Pneumology Dept, University and Politechnic La Fe Hospital, Bulevar Sur s/n, Valencia, 46013, Spain. E-mail: mianmartinezgarcia@gmail.com

 Print ISBN: 978-1-84984-118-4. Online ISBN: 978-1-84984-119-1. Print ISSN: 2312-508X. Online ISSN: 2312-5098.

Diseases such as lung cancer and the intermittent hypoxaemia or sleep fragmentation caused by OSA can influence the cardiovascular system, either by spreading or by secreting biological mediators or implementing mechanisms that have been proven to cause vascular damage.

Finally, although the therapies used for the management of respiratory diseases are generally effective and safe, it is well known that many of the adverse effects of drugs, used in the management of pulmonary diseases, such as bronchodilators, corticosteroids, antibiotics, antifibrotics, anticoagulants, anti-tumoral and anti-inflammatory therapies, may incorporate a degree of cardiovascular risk, particularly in some particularly susceptible patients.

In this *ERS Monograph*, we have tried to offer the reader a complete overview of the interaction between pulmonary diseases and CVDs, not only from an epidemiological point of view [1], but also from a pathophysiological [2], and more particularly, clinical and therapeutic point of view. Accordingly, after reviewing some basic concepts, the book has been divided into: firstly, each important group of respiratory diseases and their cardiopulmonary implications [3–14]; then to the groups of drugs most used in pulmonology and their potential cardiovascular effects [15–19]; and finally, to future diagnostic challenges in this field [20]. Three clinical cases have also been chosen to illustrate different situations taken from real life, in order to delve more fully into the concepts discussed in this book [21–23].

We hope that this *Monograph* provides you with some of the answers to the questions you have asked in daily practise when trying to diagnose and treat complex patients who suffer from both cardiovascular and respiratory pathology. That was our main objective.

References

1. Soriano JB, Elosua R. Epidemiological aspects of cardiovascular and respiratory diseases. *In*: Martínez-García MA, Pépin J-L, Cazzola M. Cardiovascular Complications of Respiratory Disorders (ERS Monograph). Sheffield, European Respiratory Society, 2020; pp. 1–11.
2. Viglino D, Maltais F, Tamisier R. Common pathophysiological pathways of the autonomic nervous system. *In*: Martínez-García MA, Pépin J-L, Cazzola M. Cardiovascular Complications of Respiratory Disorders (ERS Monograph). Sheffield, European Respiratory Society, 2020; pp. 12–30.
3. Rogliani P, Calzetta L. Cardiovascular disease in COPD. *In*: Martínez-García MA, Pépin J-L, Cazzola M. Cardiovascular Complications of Respiratory Disorders (ERS Monograph). Sheffield, European Respiratory Society, 2020; pp. 47–65.
4. Ora J, Cavalli F, Cazzola M. Management of patients with asthma or COPD and cardiovascular disease: risks *versus* benefits. *In*: Martínez-García MA, Pépin J-L, Cazzola M. Cardiovascular Complications of Respiratory Disorders (ERS Monograph). Sheffield, European Respiratory Society, 2020; pp. 66–81.
5. Argueta FA, Alviar CL, Peters JI, *et al.* Chronic asthma and the risk of cardiovascular disease. *In*: Martínez-García MA, Pépin J-L, Cazzola M. Cardiovascular Complications of Respiratory Disorders (ERS Monograph). Sheffield, European Respiratory Society, 2020; pp. 82–95.
6. Guan W-j, Gao Y-h, de la Rosa-Carillo D, *et al.* Cardiovascular implications in bronchiectasis. *In*: Martínez-García MA, Pépin J-L, Cazzola M. Cardiovascular Complications of Respiratory Disorders (ERS Monograph). Sheffield, European Respiratory Society, 2020; pp. 96–107.
7. Downey DG, Elborn JS. Cardiovascular complications of cystic fibrosis. *In*: Martínez-García MA, Pépin J-L, Cazzola M. Cardiovascular Complications of Respiratory Disorders (ERS Monograph). Sheffield, European Respiratory Society, 2020; pp. 108–117.
8. Bonsignore MR, Gallina S, Drager LF. Cardiovascular consequences of sleep disordered breathing: the role of CPAP treatment. *In*: Martínez-García MA, Pépin J-L, Cazzola M. Cardiovascular Complications of Respiratory Disorders (ERS Monograph). Sheffield, European Respiratory Society, 2020; pp. 118–142.

 https://doi.org/10.1183/2312508X.10005220

Disclosures: None declared.

List of abbreviations

AA	atrial arrhythmias
AF	atrial fibrillation
AFL	atrial flutter
AHI	apnoea–hypopnoea index
BMI	body mass index
BP	blood pressure
CAC	coronary artery calcification
CAD	coronary artery disease
CHF	chronic heart failure
CPAP	continuous positive airway pressure
CVD	cardiovascular disease
CVE	cardiovascular event
D_{LCO}	diffusing capacity of the lung for carbon monoxide
FEV_1	forced expiratory volume in 1 s
FVC	forced vital capacity
HF	heart failure
ICS	inhaled corticosteroid
IHD	ischaemic heart disease
IL	interleukin
ILD	interstitial lung disease
IPF	idiopathic pulmonary fibrosis
MACE	major adverse cardiac event
mPAP	mean pulmonary arterial pressure
OSA	obstructive sleep apnoea
PAH	pulmonary arterial hypertension
PAP	pulmonary arterial pressure
PH	pulmonary hypertension
RHC	right heart catheterisation
TNF	tumour necrosis factor
VEGF	vascular-endothelial growth factor