
The Pathology of Cardiac Transplantation

Ornella Leone • Annalisa Angelini
Patrick Bruneval • Luciano Potena
Editors

The Pathology of Cardiac Transplantation

A Clinical and Pathological
Perspective

 Springer

Editors

Ornella Leone
Cardiovascular and Cardiac Transplant
Pathology Program
Department of Pathology
Sant'Orsola-Malpighi University Hospital
Bologna
Italy

Annalisa Angelini
Pathology of Cardiac Transplantation
and Regenerative Medicine Unit
Department of Cardiac
Thoracic and Vascular Sciences
University of Padua
Padua
Italy

Patrick Bruneval
Department of Pathology
Hôpital Européen Georges Pompidou
Paris
France

Luciano Potena
Heart Failure and Heart Transplant
Program, Cardiology Unit
Sant'Orsola-Malpighi University
Hospital
Bologna
Italy

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To all those who generously donate their organs, to patients on the waiting list and to all transplanted patients

And to all the health professionals, too numerous to mention by name, who with their hard and dedicated work make transplantation possible

Foreword

Nearly 50 years have elapsed since Christian Barnard in Cape Town accomplished what was considered a breakthrough in medicine and cardiac surgery, namely treatment of terminal congestive cardiac failure with the replacement of the whole heart.

Richard Lower and Norman Shumway had previously done fundamental experimental work on large animals at Stanford and deserve a great part of the merit for this achievement, but the brilliant young surgeon from South Africa had the nerve to do it directly with humans. However, at that time, the barrier of immunologic tolerance was not yet resolved, and the first transplants were complicated by severe cellular rejection and graft failure. The Stanford team continued with the experimental work and in the 1980s, with the discovery and clinical application of cyclosporine, which could control T-cell immune reaction, cardiac transplantation entered into clinical practice worldwide with striking success (approximately 95% hospital survival, 75% still alive at 10 years follow-up).

Why was heart transplantation the dawn of contemporary cardiovascular pathology? For several reasons, well documented in the *Treatise of Pathology of Cardiac Transplantation* by Leone et al.

With transplantation, cardiac pathologists started to play a key role in diagnosis and prognosis for live patients, in close collaboration with clinicians. They moved from the anatomical to the surgical theater, from the mortuary table to the operating table, restoring health. The days were over when the cardiac pathologist only witnessed the natural end of the human body or clinical failure and when the meaning and mission of his job was “... *mors gaudet succurrere vitae*” (... death’s joy in helping future lives). He became a guardian of life.

On that memorable night of November 14, 1985, in Padua, Prof. Vincenzo Gallucci carried out the first cardiac transplantation in Italy and, for the first time, I held in my hands a still beating heart, a specimen from a living patient. It was a turning point in my career. A series of successful transplantations followed, requiring weekly rejection monitoring through endomyocardial biopsy. My mind flies back to the memory of Margaret Billingham, the teacher and mentor of generations of cardiovascular pathologists in cardiac transplant centers worldwide.

In the arena of cardiac transplantation, the pathologist plays several key roles:

- (a) Before operation, with diagnostic endomyocardial biopsy, to establish cause of morbidity leading to heart failure so severe as to require the extreme option of heart replacement.

- (b) During operation, with manipulation and sampling of the cardiac specimens for precise diagnosis and molecular investigation.
- (c) After operation, in the follow-up, with periodic endomyocardial biopsies for rejection monitoring and, in case of fatal outcome, with the usual necropsy to ascertain causes and mechanisms of failure (early multiorgan failure, recurrent acute rejection, infections, lympho-proliferative disorders, late allograft rejection). For all of us it has been a unique training experience, from gross anatomy and light or electron microscopy to infective or genetic molecular pathology.

Previously unknown diseases were discovered in the “gymnasium” of cardiac transplantation. For instance, primary restrictive cardiomyopathy with severe diastolic ventricular impairment and congestive heart failure, known as the “paradox of small heart requiring transplantation”. It was eventually discovered to be genetically determined sarcomere disease.

This book has been very well orchestrated and written by a team of international experts, including pathologists, clinicians, surgeons, and immunologists. To the best of my knowledge, this is the first comprehensive treatise in the field. All the issues regarding the discipline of cardiac transplantation are covered: epidemiology of congestive cardiac failure, indication to transplant including diagnostic endomyocardial biopsy, donation and graft preservation, graft failure, immunology of cellular and humoral rejection, infective and neoplastic complications, and chronic rejection as allograft vasculopathy. Last but not least, artificial support for a failing heart with ventricular assistance devices as a bridge to transplant or destination therapy.

This book looks wonderful, enriched with beautiful illustrations, a true encyclopedia of cardiac transplantation. Let me express my congratulations to the Editors, who have been the conductors of a concert of eminent scholars in the field.

Pathology and pathologists are back again in the core of cardiovascular medicine.

Gaetano Thiene, MD,
Honorary FRCP London,
Professor of Pathology,
University of Padua,
Padua,
Italy

Preface

Today heart transplantation is an acknowledged therapy for the treatment of end-stage heart failure and is still the gold standard procedure for a selected group of patients with terminal heart failure: the 5-year survival rate is an impressive 71.7%.

The major limiting factor is donor shortage. In addition, in recent years, the heart donor pool has had a more complex profile due to the presence of older donors with co-morbidities and the progressive shift from young and healthy trauma victims to brain death donors, which may cause adverse haemodynamic cardiac events. The decreasing number of donor hearts and the growing number of heart failure patients contribute to the substantial mortality rate in waiting list patients. Over the past two decades, this shortfall has exacerbated the need to extend criteria for organ acceptability by considering marginal/higher-risk donors, including older donors, as they represent a potential immediate increase in the number of suitable hearts.

After the pioneering era of the first heart transplantation in 1967, it became clear that this new and complex medical context called for a multidisciplinary work-up model where the various specialists involved can work closely together in standardizing diagnostic and therapeutic strategies or in research and specialist training. There was also work to be done in familiarizing the public with the very idea of heart donation.

The cardiovascular pathologist is part of this multidisciplinary team and works closely together with clinicians and surgeons and other specialists throughout the entire transplant process, thus emerging from the isolation in which the pathologists often find themselves.

This book has the backing of the Association for European Cardiovascular Pathology (AECVP) (www.aecvp.org), which was founded in 2001 as a development of the European School for Cardiovascular Pathology, founded in 1994.

AECVP aims to bring together “those in Europe actively involved in cardiovascular pathology and provides a platform to serve as a liaison between pathologists, cardiologists and surgeons as well as basic science researchers in the field of cardiovascular diseases”. Its purpose is to be “instrumental in coordinating many aspects of cardiovascular pathology in Europe, such as quality control studies in the diagnostic field and in the implementation of multicentre studies in the cardiovascular pathology arena” and to “put much emphasis on mutual postgraduate education programs”.

The AECVP developed a close liaison with the European Society of Pathology and participates as companion society in the annual European

Congress of Pathology meetings. AECVP regularly collaborates with the sister North American Society for Cardiovascular Pathology (SCVP) and other European scientific societies, such as the European Society of Cardiology, International Academy of Forensic Medicine and European Association for Cardio-Thoracic Surgery.

In 2008, the Association initiated a Cardiac Transplant Working Group to highlight the fact that heart transplant pathology lies within the wider discipline of cardiovascular pathology. This led to the development of a European Heart Transplant Network (whose membership currently stands at 50), in order to create an effective liaison with pathologists working in cardiac transplantation, to compare experience and exchange information on local practice and organization, as well as to develop educational programmes, reproducibility studies and online collaborative projects on cardiac transplant pathology. The European Transplant Group also collaborates with the International Society for Heart and Lung Transplantation (ISHLT) and its Pathology Council, with the Banff Foundation for Allograft Pathology and with the European Society for Solid Organ Transplantation (ESOT) and its Cardio-Thoracic Section (ECCTA), in order to develop guidelines and multi-center studies.

The book was conceived with the purpose of focusing on pathology issues in cardiac transplantation in a clinical perspective, with emphasis on the value of multidisciplinary team-work and collaborative research. Its intention is to provide a scientific framework with a comprehensive review of the chronological phases of the transplant process, up-to-date pathological protocols and classification schemes and a step-by-step approach to guide the reader. The principal points are the need for constant dialogue between the pathologist and the clinician and the need to build on what we have achieved and to continue working together to illuminate the grey areas that remain.

Bologna, Italy
Padua, Italy
Paris, France
Bologna, Italy

Ornella Leone
Annalisa Angelini
Patrick Bruneval
Luciano Potena

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Contributors

Valentina Agostini, MD Department of Pathology, Sant'Orsola-Malpighi University Hospital, Bologna, Italy

Annalisa Angelini, MD Pathology of Cardiac Transplantation and Regenerative Medicine Unit, Department of Cardiac, Thoracic and Vascular Sciences, University of Padua, Padua, Italy

Klaus Aumayr, MD Clinical Institute for Pathology, Medical University of Vienna, Vienna, Austria

Jonida Bejko, MD, PhD Division of Cardiac Surgery, Department of Cardiac, Thoracic and Vascular Sciences, University of Padua, Padua, Italy

Gerald J. Berry, MD Department of Pathology, Stanford Medical Center, Stanford, CA, USA

Patrick Bruneval, MD Department of Pathology, Hôpital Européen Georges Pompidou, Paris, France

Margaret Burke, MB, FRCPath Department of Histopathology, Harefield Hospital, Royal Brompton and Harefield NHS Trust, London, UK

Brian A. Clarke, MD Division of Cardiology, Department of Medicine, Dalhousie University and the QE II Health Science Center, Halifax, NS, Canada

Julien Coussement, MD Division of Infectious Diseases, CUB-Erasme, Université Libre de Bruxelles, Brussels, Belgium

Maria Crespo-Leiro, MD, PhD, FESC, FHFA Unidad de Insuficiencia Cardíaca Avanzada y Trasplante Cardíaco, Servicio de Cardiología, Complejo Hospitalario Universitario A Coruña e Instituto de Investigación Biomédica (INIBIC) A Coruña, A Coruña, Spain

Carlo Dal Lin, MD Cardiology Unit, Department of Cardiac, Thoracic and Vascular Sciences, University of Padua, Padua, Italy

Helen Doran, FRCPath Department of Histopathology, University Hospitals of South Manchester NHS Foundation Trust, Manchester, UK

- Jean-Paul Duong Van Huyen, MD, PhD** Department of Pathology, University Paris-Descartes, Hôpital Necker-Enfants Malades, Paris, France
- Volkmar Falk, MD, PhD** Department of Cardiothoracic and Vascular Surgery, German Heart Institute Berlin, Berlin, Germany
- Marny Fedrigo, MD, PhD** Cardiovascular Pathology Unit, Department of Cardiac, Thoracic and Vascular Sciences, Azienda Ospedaliera Padua, Padua, Italy
- Giuseppe Feltrin, MD, PhD** Operative Unit of the Regional Center for Transplant Coordination, University of Padua, Padua, Italy
- Gerasimos Filippatos, MD, FESC, FACC** Heart Failure Unit, Department of Cardiology, Athens University Hospital, Athens, Greece
- Alberto Foà, MD** Department of Cardiology, Sant'Orsola-Malpighi University Hospital, Bologna, Italy
- Gino Gerosa, MD** Division of Cardiac Surgery, Department of Cardiac, Thoracic and Vascular Sciences, University of Padua, Padua, Italy
- Martin Goddard, FRCS, MRCPATH** Department of Pathology, Papworth Hospital NHS Trust, Cambridge, UK
- Heike Goebel, MD** Institute of Pathology, University of Cologne, Köln, Germany
- Francesco Grigioni, MD, PhD** Heart Failure and Heart Transplant Program, Cardiology Unit, S.Orsola-Malpighi University Hospital, Bologna, Italy
- Franck Iserin, MD** Department of Pediatric Cardiology, Hôpital Necker-Enfants Malades, Paris, France
- Spyridon Katsanos, MD** Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands
- Abdallah G. Kfoury, MD** Division of Cardiovascular Disease, Intermountain Medical Center, Utah Transplant Affiliated Hospitals (U.T.A.H.) Cardiac Transplant Program, Murray, UT, USA
- Kiran K. Khush, MD, MAS** Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA, USA
- Thomas Krabatsch, MD, PhD** Department of Cardiothoracic and Vascular Surgery, German Heart Center Berlin, DZHK (German Center for Cardiovascular Research), Partner Site Berlin, Berlin, Germany
- David Lebeaux, MD** Université Paris Descartes, Sorbonne Paris Cité, AP-HP, Hôpital Necker Enfants Malades, Centre d'Infectiologie Necker-Pasteur and Institut Imagine, Paris, France
- Ornella Leone, MD** Cardiovascular and Cardiac Transplant Pathology Program, Department of Pathology, Sant'Orsola-Malpighi University Hospital, Bologna, Italy

Olivier Lortholary, MD, PhD Université Paris Descartes, Sorbonne Paris Cité, AP-HP, Hôpital Necker Enfants Malades, Centre d'Infectiologie Necker-Pasteur and Institut Imagine, Paris, France

Gaia Magnani, MD, PhD Heart Failure and Heart Transplant Program, Cardiology Unit, S.Orsola-Malpighi University Hospital, Bologna, Italy

Valentina Manfredini, MD Heart Failure and Heart Transplant Program, Cardiology Unit, S.Orsola-Malpighi University Hospital, Bologna, Italy

Francesco Marchini, MD II Nephrology Unit, Azienda Ospedaliera-Universitaria Padova, Padua, Italy

Marco Masetti, PhD Heart Failure and Heart Transplant Program, Cardiology Unit, S.Orsola-Malpighi University Hospital, Bologna, Italy

Dylan V. Miller, MD Intermountain Central Lab, University of Utah, Salt Lake City, UT, USA

Desley A.H. Neil, MD Department of Histopathology, Medical School University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

Marie-Claude Parent, MD, MSc, FRCPC Division of Cardiology, Hôpital du Sacré-Coeur de Montréal, Université de Montréal, Montréal, Québec, Canada

John T. Parissis, MD, FESC Heart Failure Unit, Cardiology Department, Attikon University Hospital, Athens, Greece

Sergei Pepoyan, MD Department of Cardiology, YSMU Hospital Complex N1, Yerevan, Armenia

Sylvain Poiree, MD Service de Radiologie Adulte, Hôpital Necker-Enfants Malades, Assistance Publique-Hôpitaux de Paris, Paris, France

Jorge Pombo-Otero, MD Cardiac Pathology Department, Complejo Hospitalario Universitario A Coruña, A Coruña, Spain

Evgenij Potapov, MD, PhD Department of Cardiothoracic and Vascular Surgery, German Heart Institute Berlin, Berlin, Germany

Luciano Potena, MD, PhD Heart Failure and Heart Transplant Program, Cardiology Unit, S.Orsola-Malpighi University Hospital, Bologna, Italy

Alexandra J. Rice, BA, MB, BChir, MRCPath Department of Histopathology, Royal Brompton Hospital, Royal Brompton and Harefield NHS Trust, London, UK

Marlene L. Rose, BSc, MSc, PhD National Heart and Lung Institute, Imperial College, Heart Science Centre, Harefield Hospital, Middlesex, UK

Samuel Rotman, MD Institute of Pathology, University Hospital of Lausanne, Lausanne-CHUV, Switzerland

John D. Smith, FRCPath Tissue Tying Laboratory, Harefield Hospital, Harefield, Middlesex, UK

Alexander Stepanenko, MD Department of Cardiothoracic and Vascular Surgery, German Heart Institute Berlin, Berlin, Germany

Francesco Tona, MD, PhD Cardiology Unit, Department of Cardiac, Thoracic and Vascular Sciences, University of Padua, Padua, Italy

Claire Toquet, MD, PhD Department of Pathology, Hôpital Hôtel-Dieu, Nantes, France

Allard van der Wal, MD, PhD Department of Pathology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

Marialuisa Valente, MD Pathological Anatomy, Department of Cardiac, Thoracic and Vascular Sciences, University of Padua, Padua, Italy

John P. Veinot, MD, FRCPC Department of Pathology and Laboratory Medicine, The Ottawa Hospital, Ottawa, ON, Canada

Aryan Vink, MD, PhD Department of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands

Katarina Wassilew, MD, DScMed Department of Pathology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

Andreas Zuckermann, MD Cardiac Transplantation Program, Department of Cardiac Surgery, Medical University of Vienna, Vienna, Austria